



Case report

Xanthogranulomatous cholangitis mimicking cholangiocarcinoma: Case report and review of literature

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ABSTRACT

Introduction: Xanthogranulomatous cholangitis is an extremely rare diagnosis and is believed to be an extension of xanthogranulomatous cholecystitis, a benign inflammatory process characterized by lipid-laden foamy macrophages (called “xanthoma cells”) occurring in a background of chronic inflammation consisting of lymphocytes, plasma cells, and eosinophils. Here, we report a case of xanthogranulomatous cholangitis mimicking cholangiocarcinoma.

Case presentation: A 72 year old male with history of recurrent cholangitis had preoperative workup highly suggestive of intrahepatic cholangiocarcinoma. He underwent right hepatectomy and portal lymphadenectomy, with pathology showing xanthogranulomatous cholangitis, with no evidence of malignancy. Interestingly, the patient did not have xanthogranulomatous cholecystitis.

Discussion: We reviewed the current literature on xanthogranulomatous cholangitis, and identified only 14 previously reported cases. In our case series, there were six female and eight male patients. Among the 14 patients, 11 presented to the hospital with jaundice. Twelve patients had preoperative workup concerning for malignancy. The diagnosis of xanthogranulomatous cholangitis was confirmed through pathology in 13 patients, and through endoscopic ultrasound biopsy in one patient. In our review, seven patients had associated xanthogranulomatous cholecystitis, three patients had an isolated case of xanthogranulomatous cholangitis, and four patients had unknown status. Our patient is the fourth case of isolated xanthogranulomatous cholangitis without xanthogranulomatous cholecystitis.

Conclusion: Xanthogranulomatous cholangitis is a very rare phenomenon that can lead to benign strictures of the bile ducts, especially in the setting of recurrent cholangitis. It can mimic malignancies, such as cholangiocarcinoma, and should be considered in the differential diagnosis.

1. Introduction

Xanthogranulomatous inflammation is a rare, benign inflammatory process that can occur anywhere in the body, including the kidney and gallbladder. It is characterized histologically by lipid-laden macrophages, lymphocytes, plasma cells, eosinophils, and fibrosis. Xanthogranulomatous cholecystitis is believed to be caused by extravasation of bile into the gallbladder wall, leading to an inflammatory reaction that involved phagocytosis of bile pigment by macrophages, resulting in the formation of xanthoma cells. Xanthogranulomatous cholangitis is theorized to be an extension of the xanthogranulomatous cholecystitis

into the bile ducts [1]. The diagnosis of xanthogranulomatous cholangitis is difficult to establish. Here, we present a case of isolated xanthogranulomatous cholangitis, without xanthogranulomatous cholecystitis, mimicking cholangiocarcinoma. This case is reported in line with the SCARE criteria [2] and PROCESS 2020 guidelines [3].

2. Presentation of a case

A 72-year-old male who was previously admitted to a tertiary academic hospital for gallstone pancreatitis, recurrent cholangitis managed with endoscopic retrograde cholangiopancreatography (ERCP), and

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Klebsiella bacteremia underwent interval laparoscopic cholecystectomy with liver biopsy. Upon insufflation of his abdomen, it was noted that his gallbladder was tense, distended, and extrahepatic. Cholecystectomy was performed without any complications. Pathology of his gallbladder revealed chronic cholecystitis and pathology of his liver biopsy was negative for fibrosis, steatosis and inflammation. His postoperative course was complicated by continued night sweats, unintentional weight loss, and jaundice. He underwent ERCP with exchange of common bile duct stents multiple times with no alleviation of symptoms.

On workup, his liver function tests remained mildly elevated (Total bilirubin 1.3 MG/DL, Aspartate Aminotransferase (AST) 78 IU/L, Alanine Aminotransferase (ALT) 64 IU/L, Alkaline Phosphatase 673 IU/L). His carcinoembryonic antigen (CEA) was normal at 1.1 NG/ML but carbohydrate antigen 19-9 (CA19-9) was significantly elevated at 160 U/ML. A computed tomography (CT) scan of abdomen/pelvis showed new intrahepatic ductal dilation and portal vein thrombus without evidence of a liver mass (Fig 1A). Magnetic resonance cholangiopancreatography (MRCP) demonstrated irregular, biliary ductal dilatation. ERCP with SpyGlass revealed right hepatic system under-filling, narrowing of the right intrahepatic duct takeoff, and abnormal biliary tract mucosa characterized by nodularity, scarring, purulence, and decreased vascularity (Fig 1B). Cytology of the right main hepatic duct showed atypical cells. As a result, there was high clinical suspicion of early intrahepatic cholangiocarcinoma. After extensive discussion with patient, he was consented for liver resection.

The patient subsequently underwent right hepatectomy and portal lymphadenectomy (Fig 2A). His pathology showed xanthogranulomatous cholangitis of large hepatic bile ducts, bile granuloma, hepatic parenchyma with features of large bile duct obstruction, chronic cholestasis, and biliary pattern of fibrosis with bridging septa (Fig 2B). There was no evidence of malignancy. Dedicated stains for bacteria and fungi were negative. He was discharged home on postoperative day 4.

He subsequently developed recurrent perihepatic abscesses managed with image guided drain placements and right pleural effusions managed with pigtail chest tube placements. Cultures from his perihepatic abscesses were positive for *Klebsiella* for which he had completed a course of intravenous ertapenem. At his last clinic follow up, patient reported doing well.

3. Discussion

Xanthogranulomatous cholangitis is an extremely rare disorder. A

literature review on Pubmed revealed only 14 previously identified cases (Table 1). In our review, six patients were female and eight were male. The most common presenting symptom for patients was jaundice (11 patients) with concern for cholangitis in five patients. Three patients presented with abdominal pain. One patient was asymptomatic and was found to have an incidental finding of hepatic mass on CT scan. Among the patients, nine had elevated bilirubin (ranges 3.2 to 23 MG/DL), and two had normal bilirubin. For 12 patients, there was preoperative diagnosis concerning for malignancy which included primary hepatic neoplasm, pancreatic cancer, gallbladder cancer, and cholangiocarcinoma. Among these 12 patients, 10 of them had imaging suggestive of malignancy while two had cytology suggestive of malignancy. Thirteen patients had surgical resections including pancreaticoduodenectomy (3 patients), hepatic resections (4 patients), bile duct resections with hepaticojejunostomy (4 patients), and resection of a hilar mass with hepaticoduodenostomy (1 patient). In one patient, the diagnosis of xanthogranulomatous cholangitis was confirmed by endoscopic ultrasound.

Interestingly, seven patients had concurrent diagnosis of xanthogranulomatous cholecystitis. There had only been three previously recorded cases of isolated xanthogranulomatous cholangitis without cholecystitis, with our patient being the fourth case. The etiology of isolated xanthogranulomatous cholangitis is unknown. In patients with concurrent xanthogranulomatous cholecystitis, it has been hypothesized to be an extension of the inflammatory reaction from the gallbladder into the bile ducts [1]. In isolated cases of xanthogranulomatous cholangitis, the bile duct wall is infiltrated with foamy macrophages leading to inflammation, fibrosis, and scarring [4]. Perhaps, in this patient, it is secondary to his recurrent episodes of cholangitis, leading to chronic bile duct inflammation, scarring, and a xanthogranulomatous reaction.

The diagnosis of xanthogranulomatous cholangitis is also elusive, with most of the diagnoses confirmed only after pathologic examination of specimens following surgical resection. However, several CT and MRI findings have been correlated with xanthogranulomatous cholecystitis [5]. Zhao et al determined that CT features of diffuse gallbladder wall thickening, intramural hypo-attenuated nodules, and luminal surface enhancement are associated with xanthogranulomatous cholecystitis [6]. Shuto et al. concluded that hypo-attenuated nodules on CT corresponds to either xanthogranuloma consisting of foamy histiocytes or abscess/necrosis [7]. MRI can further differentiate xanthogranuloma from abscess/necrosis. On MRI, areas of isoto-high signal intensity on T2 weighted images that have slight enhancement on early and strong

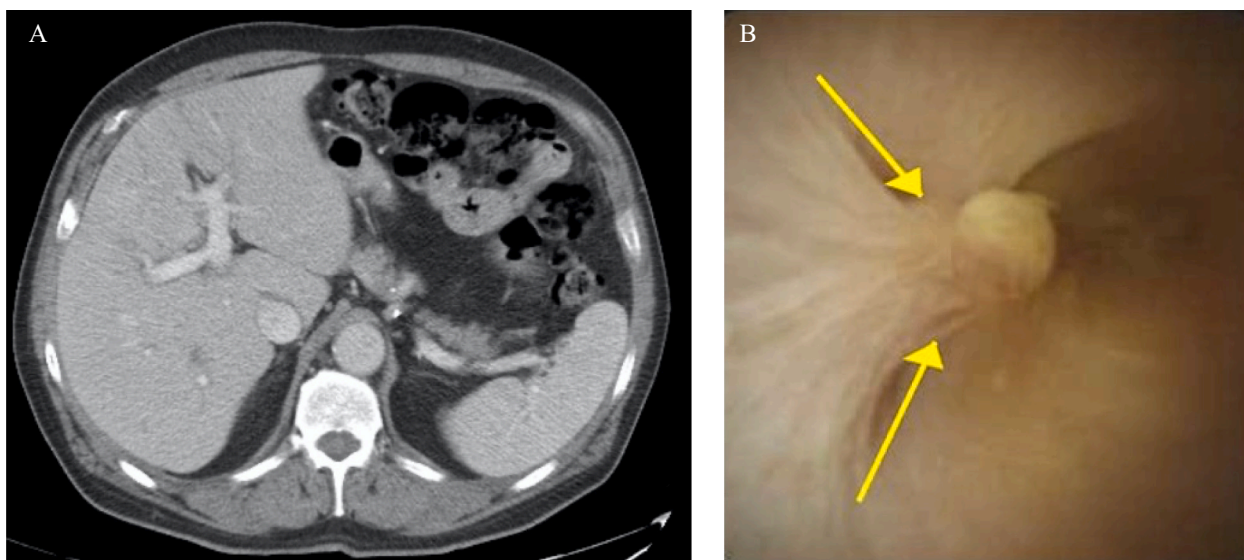


Fig. 1. A. CT abdomen/pelvis showing significant intrahepatic biliary ductal dilatation B. ERCP with SpyGlass showing nodularity at the right main hepatic duct.

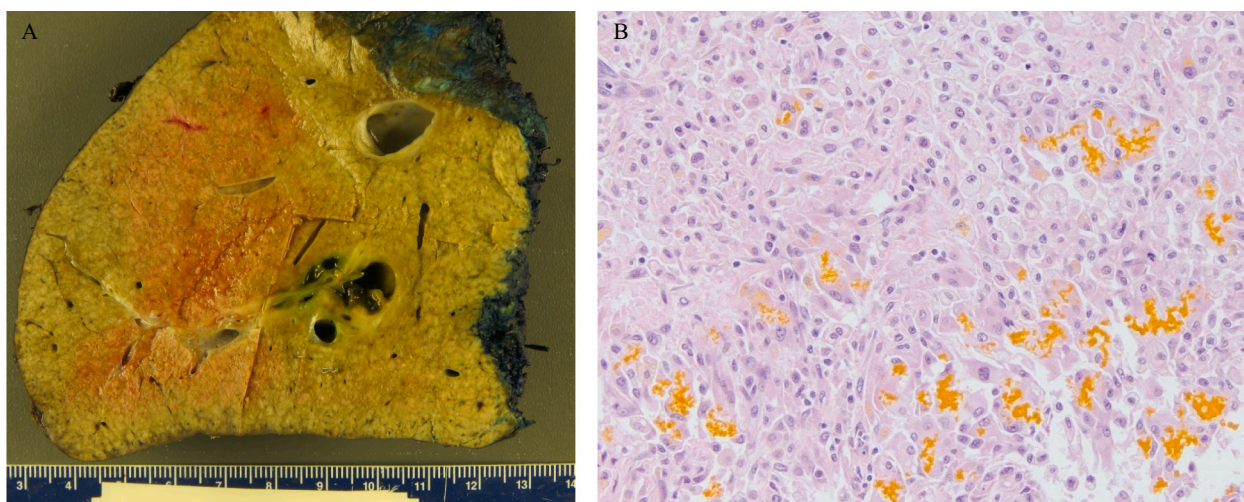


Fig. 2. A. Gross specimen of the right lobe of liver B. High power view showing characteristic xanthoma cells, the lipid-laden foamy macrophages which display an eosinophilic to clear, vacuolated or granular cytoplasm, some seen here with ingested bile.

Table 1
Previously reported cases of xanthogranulomatous cholangitis.

Reference	Age	Sex	Presenting symptoms	Bilirubin (MG/DL)	Preoperative diagnosis	Operation	Diagnosis	Xanthogranulomatous cholecystitis
Goldar-Najafi et al. [9]	56 yo	F	Abd pain	wnl	Imaging suggestive of hepatic malignancy	Liver resection	Pathology	Unknown
	45 yo	M	Jaundice	4.4	Imaging suggestive of pancreatic malignancy	Pancreaticoduodenectomy	Pathology	Unknown
Pantanowitz et al. [10]	75 yo	F	Recurrent cholangitis		Imaging suggestive of cholangiocarcinoma	L hepatic segmentectomy, CCY	Pathology	Unknown
Kawate et al. [11]	34 yo	F	Jaundice	7.5	Bile cytology suggestive of class V adenocarcinoma	Extended R hepatectomy, extrahepatic bile duct resection	Pathology	No
	55 yo	M	Jaundice, cholangitis	11.7	ERCP cytology suggestive of cholangiocarcinoma	CCY, CBD excision, RNY hepaticojejunostomy	Pathology	Yes
Krishna et al. [12]	43 yo	F	Jaundice, abd pain, cholangitis	3.2	Imaging suggestive of gallbladder carcinoma/hilar cholangiocarcinoma	CCY, RNY hepaticojejunostomy	Pathology	Yes
	48 yo	F	Jaundice, cholangitis	7.9	Imaging suggestive of periampullary malignancy	Pancreaticoduodenectomy	Pathology	Yes
	56 yo	M	Jaundice, cholangitis	3.2	Imaging suggestive of hilar cholangiocarcinoma	R hepatectomy, RNY L hepaticojejunostomy	Pathology	Yes
Alsheik et al. [13]	37 yo	M	Jaundice, weight loss, diarrhea	4.4		CCY	Pathology	Yes
Jun et al. [14]	67 yo	M	Jaundice, abd pain	5.3	Imaging suggestive of pancreatic cancer	Pancreaticoduodenectomy	Pathology	No
Garg et al. [15]	32 yo	F	Jaundice, fever	23	Imaging suggestive of gallbladder cancer	Radical CCY with CBD excision, RNY hepaticojejunostomy	Pathology	Yes
Bae et al. [1]	80 yo	M	Asymp	wnl	Imaging suggestive of cholangiocarcinoma	Left lobectomy	Pathology	Unknown
Zbaida et al. [16]	9 mo	M	Jaundice		Imaging suggestive of cholangiocarcinoma	Resection of hilar mass, CCY, hepaticoduodenostomy	Pathology	No
Ikezawa et al. [17]	70s yo	M	Jaundice			None	EUS/FNA	Yes
Our patient	72 yo	M	Weight loss, abd pain, jaundice	1.3	Imaging and EUS suggestive of cholangiocarcinoma	Right hepatectomy, portal lymphadenectomy	Pathology	No

Abd = Abdominal. Asymp = Asymptomatic. CBD = Common bile duct. CCY = Cholecystectomy. F = female. L = left. M = Male. R = right. RNY = Roux-en-y. Wnl = within normal limits.

enhancement on late phase are representative of xanthogranulomas. Areas of high intensity on T2 weighted images without enhancement on early or delayed phase are representative of abscess/necrosis.

As seen in this case series, xanthogranulomatous cholangitis can mimic malignancies, such as cholangiocarcinoma. Other benign diseases that can mimic cholangiocarcinoma includes primary sclerosing cholangitis, recurrent pyogenic cholangitis, inflammatory pseudotumor, and Mirizzi syndrome [8]. It can be difficult to rule out cholangiocarcinoma preoperatively, and in many cases, surgery is needed to definitely rule

out cancer. Although rare, xanthogranulomatous cholangitis should be included in the differential diagnosis of biliary abnormalities.

4. Conclusion

We present a patient with initial workup concerning for intrahepatic cholangiocarcinoma. Following liver resection, the final pathology showed xanthogranulomatous cholangitis with no malignancy. Review of literature suggests that patients often present with jaundice, and that

many of the patients have preoperative workups concerning for malignancy. Most patients ultimately undergo surgical resection, with pathology confirming the diagnosis of xanthogranulomatous cholangitis. Even though xanthogranulomatous cholangitis is rare, it should be included in the differential diagnosis of biliary abnormalities.

Ethical approval

Not applicable.

Registration of research studies

Not applicable.

Guarantor

Jenny Zhang, Rachel Beard.

Consent

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Jenny Q. Zhang: study concept, data collection, data analysis, writing paper.

Lance Truong: data collection, data analysis, writing paper.

Jason Pan: data collection, data analysis, writing paper.

Evgeny Yakirevich: data collection, data analysis, writing paper.

Sarah M. Hyder: data collection, data analysis, writing paper.

Rachel E. Beard: data collection, data analysis, writing paper.

Declaration of competing interest

None.

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