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Case Series

XANTHOGRANULOMATOUS CHOLECYSTITIS – A RARE HISTOLOGICAL VARIANT

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ABSTRACT

Xanthogranulomatous cholecystitis is a rare presentation of chronic cholecystitis, characterized by xanthogranuloma, severe foam cells, and fibrosis. It can be an inducement of difficulty in cholecystectomy. In this case series, we describe four cases of cholecystitis which was diagnosed post-operatively to have xanthogranulomatous inflammation in the gallbladder on histopathological examination.

Keywords: Cholecystectomy, Gallbladder, Xanthogranulomatous inflammation.

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INTRODUCTION

Xanthogranulomatous cholecystitis (XGC) is a rare pathology of the gallbladder (GB) characterized by a focal or diffuse destructive inflammatory process followed by marked proliferative fibrosis along with infiltration of histiocytes, macrophages, and foamy cells [1], which was first described as XGC by McCoy *et al*. in 1976 [2,3]. Patients with XGC present typical features of acute or chronic cholecystitis, and the radiology and intraoperative findings mimic those of GB carcinoma (GBCa), leading to its frequent misdiagnosis [4], and making it difficult for surgical treatment. Moreover, this misdiagnosis also can lead to a potential misjudgment of how to excise the lesion, and if radical surgical excision is performed, it may also expand the scope of surgery and increase post-operative complications [5].

We retrospectively analyzed clinical symptoms, radiology, operation records, and histopathological findings with a pathological diagnosis of XGC who were treated in our hospital from June 2017 to July 2020.

CASE REPORT: 01

A 27-year-old female, with no known previous comorbidities, presented to the emergency department with a history of pain right side upper abdomen along with fever, nausea, and vomiting of 1-day duration. The pain was insidious onset, gradually progressive, continuous, and moderate intensity. On examination, the patient was conscious, cooperative, and oriented. She had tachycardia, P-110/min, blood pressure (BP) 124/70 mmHg, respiratory rate (RR) 18/min, and SpO_2 99% at room air. On abdomen examination, marked tenderness was present in the right hypochondrium. Murphy's sign was positive. Laboratory parameters revealed hemoglobin (Hb) of 12.1g%, total leukocyte count (TLC)-12,100/cumm, and P79L16. Her blood sugars, liver function tests (LFTs), and renal function tests (RFTs) were WNL. Ultrasound scan of the abdomen revealed acute cholecystitis with multiple small gallstones and diffuse GB wall thickening up to 9 mm (normal thickness is <3 mm) with cystic areas in the fundal wall. Contrast-enhanced computed tomography ABD/magnetic resonance cholangiopancreatography (MRCP) was not done in this case due to the non-availability of the same at our center.

The patient underwent interval laparoscopic cholecystectomy which was converted to open cholecystectomy secondary to "extensive adhesions and inflammation" after 4 weeks as per the protocol of the hospital. The adjacent liver bed was also excised due to dense adhesions of the GB with the liver bed. The intraoperative findings are as follows:

- Intrahepatic GB
- Distended GB with thickened wall
- Dense pericholecystic adhesions with liver bed and adjacent bowel loops
- Minimal pericholecystic fluid collection
- Multiple gallstones.

The surgery of the patient was uneventful. Histopathological analysis of the GB specimen with adjacent liver bed showed nodular collections of foamy macrophages in the wall of the GB admixed with histiocytes, plasma cells, and cholesterol cells. Focal chronic lymphomononuclear inflammatory infiltrate was seen in all layers up to serosa. A few Rokitansky-Aschoff (RA) sinuses were seen. There was fibrosis of underlying muscularis propria with areas of collagenization. No dysplasia/desmoplasia/malignancy was noted. Adjacent liver bed normal.

Her post-operative recovery was completely uneventful. The patient was discharged after 7 days. Her subsequent outpatient department (OPD) visits after 2 weeks and 4 weeks were unremarkable.

CASE REPORT: 02

A 51-year-old male patient, with no known previous comorbidities, presented to the emergency department history of pain right side upper abdomen along with fever, vomiting, and anorexia for 3 days duration. The pain was insidious onset, gradually progressive, continuous, and severe intensity. On examination, the patient was conscious, cooperative, and oriented. He had tachycardia, P - 106/min, BP - 154/90 mmHg, RR-18/min, SpO_2 - 99% at room air, and mild icterus was present. On abdomen examination, marked tenderness was present in the right hypochondrium. Murphy's sign was positive. Laboratory parameters revealed Hb of 17.2g%, TLC - 15,100/cumm, and P79L16. Serum bilirubin was 3.5 mg/dL (direct 2.9) with raised SGOT/SGPT and alkaline phosphatase (76/54/240). His blood sugars and RFTs were WNL. Ultrasound scan abdomen revealed acute cholecystitis with multiple small gallstones, choledocholithiasis with dilated common bile duct (CBD) (6 mm), intrahepatic biliary tree dilatation, and diffuse GB wall thickening up to 7 mm (normal thickness <3 mm). MRCP was done which revealed significant thickening of the GB wall, 1 cm in maximum width, with multiple cystic outpouchings in addition to multiple gallstones and a single CBD stone with dilated CBD around 6 mm. In addition, there was T2 hyperintensity, in the liver parenchyma surrounding the GB fossa consistent with inflammatory change. No abnormal enhancing hepatic foci were identified. Findings were felt to be consistent with

adenomyomatosis. The patient underwent endoscopic retrograde cholangiopancreatography (ERCP) with the removal of CBD stone and CBD stenting by a gastroenterologist.

The patient underwent an interval laparoscopic cholecystectomy which was converted to open cholecystectomy secondary to "extensive adhesions and inflammation" after 4 weeks as per the protocol of the hospital. The adjacent liver bed was also excised due to dense adhesions of the GB with the liver bed.

The intraoperative findings are as follows:
- Distended GB with thickened wall
- Frozen calot's triangle
- Dense adhesions of the GB with liver and colon
- Multiple gallstones.

Histopathological analysis of the GB specimen showed significant hyperplasia with fibrosis of the muscularis propria. Sheets of nodules of foamy histiocytes admixed with lymphomononuclear cells and Touton such as giant cells were seen underneath the epithelium. Occasional RA sinuses were seen. No dysplasia/evidence of malignancy was noted. His post-operative recovery was completely uneventful. The patient was discharged after 10 days. His subsequent OPD visits after 2 weeks and 4 weeks were unremarkable.

CASE REPORT: 03

A 52-year-old male patient, with no known previous comorbidities, presented to the emergency department history of pain right side upper abdomen along with nausea, vomiting, and anorexia of 7 days duration. The pain was insidious onset, gradually progressive, continuous, and moderate intensity. On examination, the patient was conscious, cooperative, and oriented. General examination revealed P - 90/min, BP - 140/90 mmHg, RR- 18/min, and SpO_2 - 99% at room air. On abdomen examination, marked tenderness was present in the right hypochondrium with a positive Murphy's sign. Laboratory parameters revealed Hb of 16.4g%, TLC - 12,600/cumm, and P65L26. His blood sugars, LFTs, and RFTs were WNL. An ultrasound scan abdomen revealed acute cholecystitis with multiple small gallstones and diffuse GB wall thickening up to 9 mm. No pericholecystic collection was seen. The liver, biliary tree, and pancreas were normal.

The patient underwent an interval laparoscopic cholecystectomy which was converted to open cholecystectomy secondary to "extensive adhesions and inflammation" after 4 weeks as per the protocol of the hospital.

The intraoperative findings are as follows:
- Thickened GB wall
- Dense adhesions of the GB with liver
- Multiple gall stones
- Normal CBD.

On histopathological analysis of the GB specimen, the mucosa was attenuated and ulcerated. There was significant hyperplasia of the muscularis propria. Nodular collection of histiocytes, giant cells, and foamy macrophages admixed with lymphomononuclear cells in the sub-epithelial tissue. Few RA sinuses were seen. No dysplasia/evidence of malignancy was noted. His post-operative recovery was completely uneventful. The patient was discharged after 2 days. His subsequent OPD visits after 2 weeks and 4 weeks were unremarkable.

CASE REPORT: 04

A 33-year-old male, with no known previous comorbidities, presented to the emergency department history of recurrent pain right side upper abdomen along with nausea, abdominal distention, and anorexia of 1-month duration. The pain was insidious onset, continuous, and mild intensity. On examination, the patient was conscious, cooperative, and oriented. General examination revealed P-85/min, BP 134/78 mmHg, RR-16/min, and SpO_2 98% at room air. On per abdomen examination, mild tenderness was present in the right hypochondrium. Murphy's sign was negative. Laboratory parameters revealed Hb of 14.4g%, TLC-9000/cumm, and P71L21. His blood sugars, LFTs with liver enzymes, and RFTs were WNL. Ultrasound scan abdomen revealed chronic cholecystitis with a single gallstone 1 cm in size and focal GB wall thickening up to 7 mm.

The patient underwent a laparoscopic cholecystectomy on admission. The intraoperative findings are as follows:
- Distended GB with thickened wall
- Densely adherent GB with liver bed
- Single gall stone
- Normal CBD.

It was a difficult cholecystectomy even though dissection and excision could be achieved laparoscopically. On histopathological analysis of the GB specimen, the mucosa was ulcerated with hyperplasia of the muscularis significant with mild hypertrophy of the lining epithelium. Intestinal metaplasia was noted at a few foci. Mild chronic lymphomononuclear inflammatory infiltrate was seen in all layers. Occasional RA sinuses were seen. No dysplasia/evidence of malignancy was noted. His post-operative recovery was completely uneventful. The patient was discharged after 2 days. His subsequent OPD visits after 2 weeks and 4 weeks were unremarkable.

DISCUSSION

XGC is a rare GB pathology showing a clinically proliferative and destructive inflammatory process, and the incidence of XGC has been reported as 0.7–13.2% of all GB-related inflammatory conditions [4,6]. XGC primarily affects older people, usually in their sixth or seventh decade of life, and suffering men and women equally [7]. Histologically, XGC is characterized by chronic inflammatory changes, with bile detected in the GB wall and macrophages engulfing lipids (Fig. 1) [8]. The most widely accepted theory for the etiopathogenesis of XGC is the rupture of the RA sinuses and the extravasation of bile into the GB wall. Extensive inflammatory fibrosis causes thickening of the GB wall and the formation of multiple yellowish-brown nodules, often spreading to adjacent organs including the liver, omentum, colon, stomach, and duodenum [9,10]. When the thickened GB wall presses against the CBD, it can often cause obstructive jaundice [11]. However, XGC is often misdiagnosed as GBCa, leading to unnecessary radical surgical excision.

In our experience, patients presented with varied clinical symptoms. 75% (3 out of 4) of patients with XGI were male. Patients with chronic

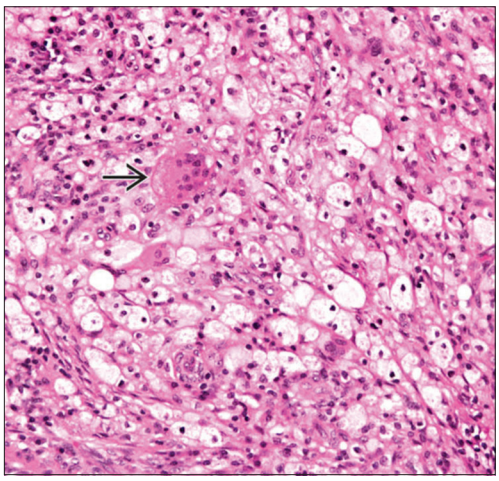

Fig. 1: Xanthogranulomatous cholecystitis showing dense infiltrate of foamy histiocytes and multinucleated giant cells are also common [11]

cholecystitis had chronic clinical presentations including chronic right upper quadrant (RUQ) pain, abdominal distension, nausea, and anorexia. Patients with acute cholecystitis presented with acute RUQ pain, nausea, vomiting, hyperpyrexia, and elevated white blood cell count.

Ultrasonography was performed in all patients, while MRCP was done pre-operatively in only 1 out of 4 patients. Focal or diffuse GB wall thickening was found in all patients on ultrasonography. Choledocholithiasis with dilated CBD and intrahepatic biliary radical dilatation was found in 1 patient which was further confirmed by MRCP followed by ERCP and stenting. Pre-operative diagnosis of xanthogranulomatous inflammation could not be made in any patient. However, there were features of adenomyomatosis GB on MRCP in one patient. 100% of patients had a difficult cholecystectomy and 75% of them underwent conversion to open procedure due to dense pericholecystic adhesions and intense inflammation. Liver bed dissection was done in 2 (50%) patients because the inflammation had extended into the liver tissues. No partial cholecystectomy was performed in this study. All the cases had a strong suspicion of GB malignancy due to intraoperative features such as dense pericholecystic adhesions and severe inflammation. All patients recovered uneventfully in this group, with no surgical site infection, pulmonary infection, or deep vein thrombosis in the post-operative period. The in-hospital stay varied from 2 to 10 days. The average in-hospital stay was 5.25 days. There was no mortality in this series.

CONCLUSION

Patients showed various clinical symptoms, ultrasonography was performed in all patients, and MRCP was further arranged selectively before the operation, but none of the patients could be pre-diagnosed. 75% of patients received open cholecystectomy. No partial cholecystectomy was performed. The intraoperative findings included cholecystolithiasis, choledocholithiasis, thickened GB wall, lesions infiltrating into adjacent tissues, and disordered calot's triangle anatomy.

CONFLICTS OF INTEREST

All authors have none to declare.

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