Section: General Surgery

Case Series

UNUSUAL CASES OF GALLBLADDER THICKENING MIMICKING CARCINOMA: A CASE SERIES

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ABSTRACT

Gallbladder wall thickening is a common yet nonspecific finding that can arise from both benign and malignant conditions.[1] Differentiating between malignancies and benign disorders such as chronic cholecystitis, cholelithiasis, xanthogranulomatous cholecystitis, and Mirizzi syndrome remains challenging due to overlapping imaging features.[2] This case series of five patients (three females, two males; ages 40-75) highlights unusual presentations of gallbladder wall thickening that closely mimicked carcinoma but were ultimately found to be benign. The series underscores the diagnostic challenges and emphasizes the importance of histopathological evaluation in distinguishing benign from malignant conditions.

Keywords: Gallbladder Malignancy, Gallbladder Thickening, Cholecystitis, Open Cholecystectomy.

INTRODUCTION

Thickening of the gallbladder wall is a frequent but nonspecific observation that may be associated with various gallbladder conditions ranging from benign inflammatory disorders to malignancies.[1] The accurate preoperative diagnosis remains challenging due to the overlap of imaging features between malignant and benign conditions such as chronic cholecystitis, cholethiasis, xanthogranulomatous cholecystitis, and Mirizzi syndrome. These benign conditions can mimic malignancy, leading to diagnostic uncertainty and impacting clinical management.[2]

In some cases, the definitive diagnosis of these conditions is only established postoperatively through histopathological evaluation. The presence of risk factors, such as gallstones, chronic inflammation, jaundice, or weight loss, often compounds the suspicion of malignancy, even in the absence of definitive radiologic evidence of invasion.[3]

This series of five cases (three females and two males ranging from 40-75 years), aims to highlight unusual cases of gallbladder wall thickening that closely mimicked carcinoma but were ultimately found to be benign conditions. These cases emphasize the importance of maintaining a high index of suspicion and the role of histopathology in distinguishing benign pathologies from malignancy. Through this case series, we explore the clinical presentation, diagnostic challenges, surgical management, and outcomes in patients who presented with features suspicious for gallbladder carcinoma but were later diagnosed with benign inflammatory conditions.

CASE-1

A 46-year-old female presented to Surgery department of Vishesh Jupiter Hospital, Indore with complaints of on and off right upper quadrant abdominal pain, described as dull and constant, occasionally radiating to the back since 5-6 months. There was no history of jaundice or fever. The patient had a history of chronic cholecystitis and cholelithiasis, diagnosed three years ago. She was advised to undergo cholecystectomy at that time but opted for conservative management. There is no history of diabetes mellitus, hypertension, or other chronic diseases. The patient had no significant family history of gallbladder disease, malignancy, or

gastrointestinal disorders. On examination, the patient appeared mildly uncomfortable due to abdominal pain. Her vital signs were stable. On abdominal examination There was moderate tenderness in the right upper quadrant, but no palpable mass or organomegaly. Murphy's sign was negative. The patient's blood investigations and Liver Function Tests were within normal limits. Ultrasonography (USG) whole abdomen revealed a thickened, calcified gallbladder wall with multiple gallstones. The calcification was extensive, creating a strong acoustic shadow. The imaging was concerning for potential malignancy due to the extent of calcification and irregular wall thickening. Contrast-Enhanced Computed Tomography (CECT) whole abdomen (as shown in Image-1[A,B]) demonstrated distended gallbladder with concentric assymetric marked thickened walls (approximately 2.5 cm.) closely approximating the hepatic flexure of colon. Multiple mixed density calculi were visualised in lumen measuring 1-1.2cm. Multiple small peri gallbladder nodes /omental nodules were also seen.

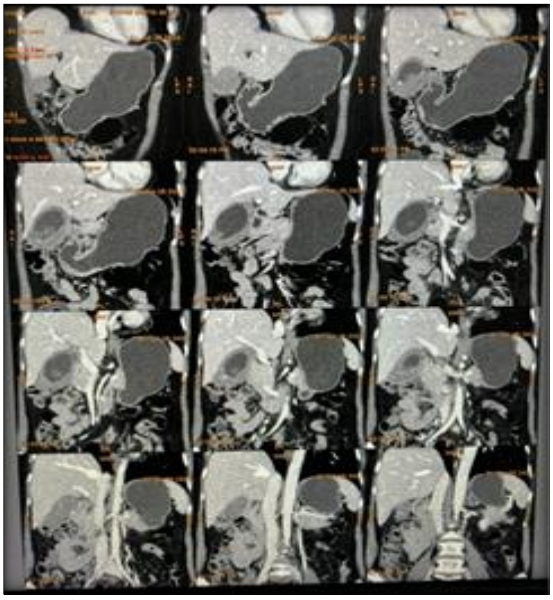

IMAGE-1 [A]

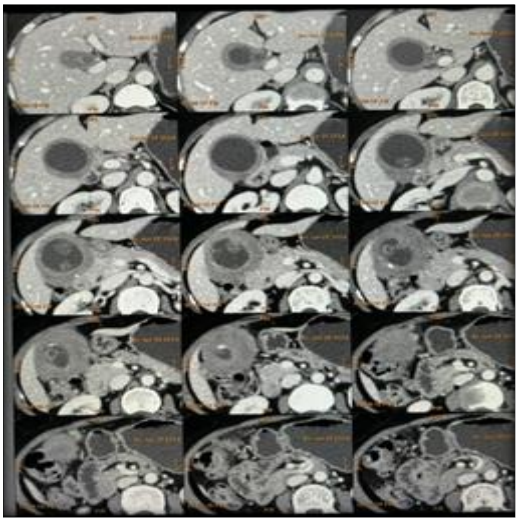

IMAGE-1 [B]

IMAGE-1 [A,B]: CECT Whole Abdomen showing diffuse thickening of gallbladder wall with multiple calculi and small peri gallbladder/omental nodes.

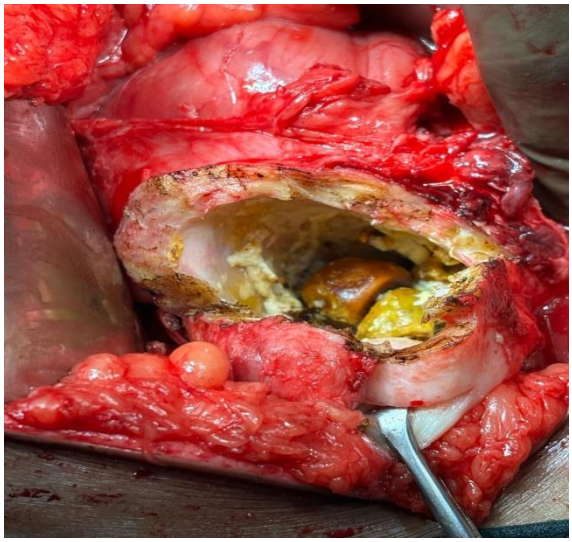

IMAGE-2: Intraoperative image showing dissected gallbladder with thickened, brittle wall along with multiple calculi.

USG guided biopsy of gallbladder fossa mass revealed hyalinized and fibrotic gallbladder with possibility of hyalinizing/ porcelain gallbladder and no evidence of malignancy. Given the high suspicion for malignancy, the patient underwent an elective open cholecystectomy. Intraoperatively, (as shown in Image-2), the dissection proved challenging due to the gallbladder being entirely thickened, brittle, and firmly adherent to the liver bed along with multiple calculi. Following the careful dissection of Calot's triangle and the division of the cystic duct and artery, the gallbladder was successfully excised.

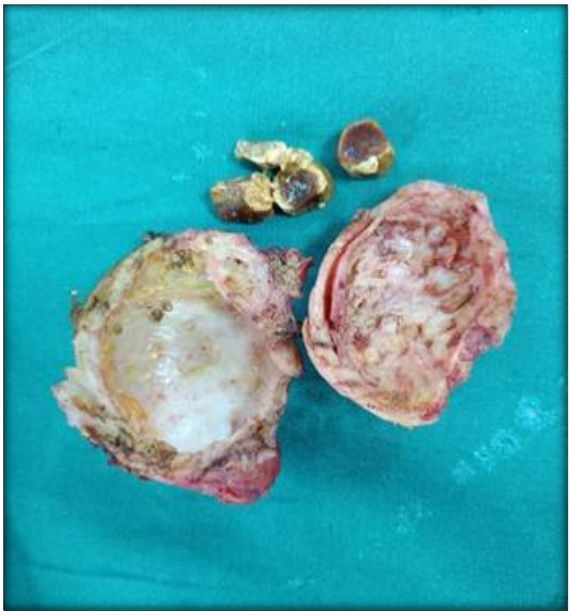

IMAGE-3 [A]

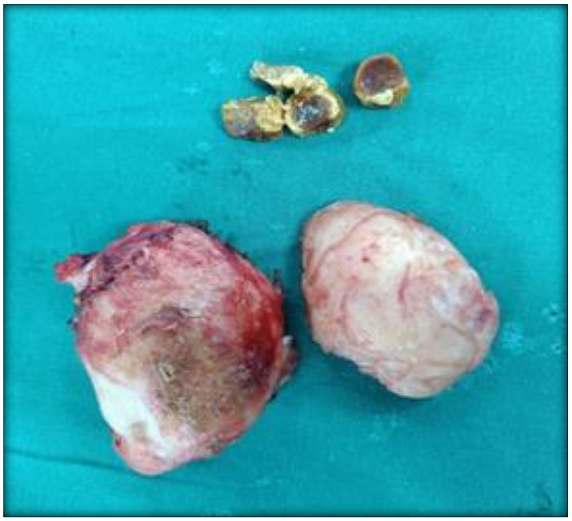

IMAGE-3 [B]

IMAGE-3[A,B]:Excised Porcelain gallbladder showing thickened walls along with multiple calculi measuring 1-1.2 cm.

Histopathological examination of the excised gallbladder (as shown in Image-3[A,B]) revealed extensive dystrophic calcification of the gallbladder wall with chronic inflammatory infiltrates, confirming the diagnosis of a porcelain gallbladder. No evidence of malignancy was found.

The surgery was successful, and her postoperative recovery was uneventful. She was discharged on the seventh postoperative day with instructions to avoid lifting heavy weights and consuming fatty meal and follow-up after seven days.

CASE-2

We hereby describe a case of a 60-year-old diabetic female, presented to a tertiary care centre with complaints of chronic right upper quadrant abdominal pain since 8 months that had progressively worsened over the past three months. The pain was dull, intermittent, and radiated to the right shoulder. She also experienced loss of appetite over the last two months. The patient had a history of jaundice three years prior, which resolved spontaneously. There is no history of hypertension or other chronic illnesses. There is no significant family history of gallbladder disease, jaundice, or malignancies. On examination, the patient appeared mildly distressed due to pain. Her vitals were stable. The abdomen was soft with marked tenderness in the right upper quadrant. Murphy's sign was positive. No palpable mass was detected.

The patient's laboratory investigations revealed a hemoglobin level of 10.5 g/dL, a white blood cell count of 13,000/mm^3 with neutrophilic predominance, and a platelet count of 300,000/mm^3. Liver function tests showed a total bilirubin level of 1.5 mg/dL (direct bilirubin: 0.8 mg/dL), elevated aspartate aminotransferase (AST) at 85 IU/L, alanine aminotransferase (ALT) at 60 IU/L, and alkaline phosphatase at 200 IU/L. Serum amylase and lipase levels were within normal limits, as were serum electrolytes. USG whole abdomen revealed a thickened gallbladder wall and hypoechoic areas. The appearance was suspicious for gallbladder malignancy due to the diffuse thickening and irregularities. CECT abdomen showed significant diffuse thickening of the gallbladder wall raising concern for gallbladder carcinoma. No definitive invasion of surrounding structures was noted, but the appearance was suggestive of malignancy. Magnetic Resonance Imaging (MRI) abdomen further demonstrated diffuse gallbladder wall thickening with low signal intensity on T2-weighted images, and no apparent invasion of adjacent organs. The findings were highly suspicious for malignancy.

The patient underwent an elective open cholecystectomy due to the strong suspicion of malignancy. However, histopathological examination of the excised gallbladder revealed findings consistent with diffuse xanthogranulomatous cholecystitis. The gallbladder wall was diffusely thickened with extensive infiltration by foamy macrophages, multinucleated giant cells, and chronic inflammatory cells. There were areas of fibrosis and necrosis. No evidence of malignancy was detected.

The surgery was uneventful, and the postoperative course was smooth. The patient was discharged on the fifth postoperative day and advised regular follow-up.

CASE-3

A 43-year-old obese female [Body Mass Index (BMI): 36 kg/m^2] presented to the surgery department with recurrent episodes of right upper quadrant abdominal pain for the past six months. The pain was sharp, intermittent, and radiating to the back and right shoulder, and relieved by analgesics. She also reported bloating, nausea, and occasional vomiting, especially after meals. There was no history of jaundice.

The patient had a history of gallstones diagnosed two years ago. She had been managing the condition conservatively. Additionally, she had been on long-term hormonal therapy, specifically oral contraceptives, for the past five years due to endometriosis. The patient's family history was unremarkable for gallbladder disease, malignancy, or gastrointestinal conditions. On physical examination, the patient appeared pale and in mild discomfort due to abdominal pain. Vital signs were stable. On systemic examination, the abdomen was soft with localized tenderness in the right upper quadrant. Murphy's sign was positive, and no palpable mass was identified. Laboratory investigations showed anemia with a hemoglobin level of 9.5 g/dL. Other results were within normal limits, including white blood cell count, platelet count, liver function tests, serum amylase, lipase, and electrolytes. USG whole abdomen revealed multiple gallstones and a thickened gallbladder wall with hypoechoic areas suggesting chronic inflammation. The findings raised concern for gallbladder malignancy due to the wall thickening and irregularities.

CECT abdomen showed gallbladder wall thickening, multiple stones, and mild pericholecystic fluid, suggestive of chronic cholecystitis. However, the irregular thickening raised suspicion for malignancy. The patient underwent open cholecystectomy with one unit packed cell transfusion.

Post-operative histopathological examination of the gallbladder specimen (as shown in Image-4) revealed chronic cholecystitis characterized by fibrosis, chronic inflammatory infiltrates, and multiple stones. No evidence of malignancy was found.

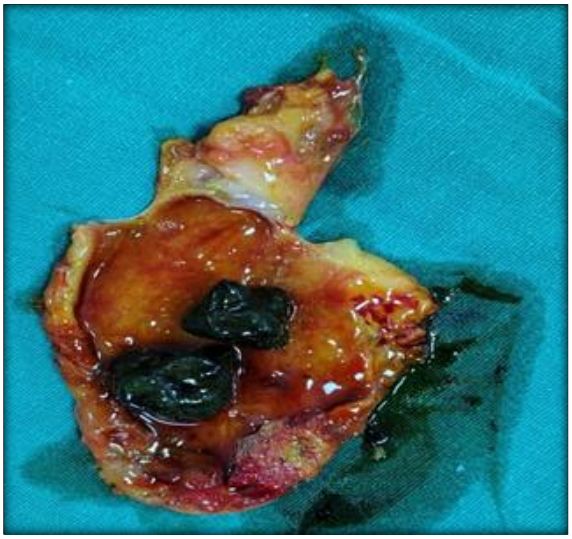

IMAGE-4: Excised thickened gallbladder showing multiple calculi

The procedure was uneventful, and she recovered well postoperatively. She was discharged on the sixth postoperative day with advice for regular follow-up.

CASE-4

A 65-year-old chronic smoker male presented with a history of recurrent episodes of dull, aching pain in the right upper quadrant for the past six months. The pain was intermittent, non-radiating, and associated with occasional nausea and postprandial bloating. He denied any history of jaundice, fever, or weight loss. The patient had a known history of hypertension, well-controlled with antihypertensive medications. There was no prior history of gallstones, liver disease, or other chronic conditions. The patient's family history was non-contributory, with no known cases of gallbladder disease, malignancy, or gastrointestinal disorders. On abdominal examination mild tenderness was noted in the right upper quadrant without any palpable mass or signs of peritoneal irritation. Murphy's sign was negative.

Laboratory investigations revealed a hemoglobin level of 13.5 g/dL, a white blood cell count of 7,800/mm^3, and a platelet count of 260,000/mm^3, all within normal limits. Liver function tests showed a total bilirubin level of 0.9 mg/dL (direct: 0.3 mg/dL), with slightly elevated aspartate aminotransferase (AST) at 45 IU/L and alanine aminotransferase (ALT) at 40 IU/L. Alkaline phosphatase was within the normal range at 100 IU/L. Serum amylase, lipase, and electrolytes were also normal. USG whole abdomen revealed circumferential thickening of the gallbladder wall without gallstones, but with the presence of dependent sludge. The wall was uniformly thickened, raising suspicion for chronic inflammation or malignancy. CECT abdomen confirmed circumferential wall thickening of the gallbladder, with no signs of local invasion or lymph node enlargement. The absence of gallstones further raised the suspicion of gallbladder carcinoma, particularly due to the fibrotic appearance.

Initially, a laparoscopic cholecystectomy was attempted. However, during the dissection, the gallbladder was found to be extremely fibrotic and hardened, making it difficult to proceed laparoscopically. The gallbladder was densely adherent to the surrounding structures, particularly the liver bed, complicating the dissection. Due to these findings, the decision was made to convert to an open cholecystectomy. Upon opening, the gallbladder was noted to be significantly fibrotic, with a thickened wall but no visible mass. The dissection of Calot's triangle was challenging due to the dense fibrosis, but the cystic duct and artery were carefully identified and divided. The gallbladder was eventually excised from the liver bed after extensive dissection, and the specimen was sent for histopathological evaluation.

Histopathological analysis revealed chronic inflammation with extensive fibrosis of the gallbladder wall, consistent with chronic cholecystitis. No evidence of malignancy was

found. The fibrosis was likely secondary to prolonged low-grade inflammation, possibly related to the presence of sludge and intermittent obstruction of the cystic duct.

The patient's postoperative recovery was uneventful. He was discharged on the fifth postoperative day with instructions for follow-up in the surgical outpatient clinic. He remained asymptomatic during the follow-up period, and no complications were noted.

CASE-5

A 75-year-old male presented with a three-month history of intermittent right upper quadrant pain, progressively worsening over the last month. The pain was sharp, radiating to the back, and accompanied by nausea, vomiting, jaundice, and unintentional weight loss of 5 kg. The patient also noticed dark urine and pale stools. The recent development of obstructive jaundice, along with the weight loss, raised concern for a possible malignancy.

The patient had a known history of gallstones since 4 years, managed conservatively. He had no prior surgical history or significant comorbid conditions, except for hypertension, which was well controlled with medication. The patient had no family history of gallbladder carcinoma or gastrointestinal malignancies. On general examination, the patient was icteric but hemodynamically stable. Vital signs were within normal limits. On abdominal examination tenderness was noted in the right upper quadrant, but no palpable mass was detected. Murphy's sign was negative. On USG the gallbladder was distended, with marked thickening of the gallbladder wall (approximately 7 mm) and multiple large gallstones, including a stone impacted in the neck of the gallbladder. There was significant dilation of the common hepatic duct, raising suspicion for gallbladder carcinoma or a malignant obstruction. CECT abdomen revealed a distended gallbladder with an irregular thickened wall. A large impacted stone was noted in the gallbladder neck, compressing the common hepatic duct, causing proximal biliary dilatation. Surrounding inflammatory changes were noted in the liver and adjacent structures. The findings were concerning for gallbladder carcinoma, possibly invading the bile duct.

MRI abdomen confirmed the thickened gallbladder wall (approximately 7.5 mm) with mixed signal intensity. A stone measuring approximately 2.3 cm impacted in the gallbladder neck, was compressing the common hepatic duct. No definitive signs of invasion were seen, but malignancy could not be ruled out. ERCP revealed extrinsic compression of the common hepatic duct by the impacted stone, consistent with Mirizzi syndrome. No intraluminal mass was found in the bile duct, but the compression mimicked a malignant stricture. Based on the clinical presentation, imaging studies, and laboratory findings, a high suspicion of gallbladder carcinoma was raised, especially due to the presence of jaundice, weight loss, and gallbladder wall thickening. However, Mirizzi syndrome was also considered due to the impacted stone in the gallbladder neck. A decision was made to proceed with open cholecystectomy. The cystic duct and artery were identified, and the gallbladder was excised. The gallbladder was found to be fibrotic with inflammatory changes, and the impacted stone was removed. Intraoperative frozen section analysis of the gallbladder wall revealed chronic inflammation with no evidence of malignancy, confirming the diagnosis of Mirizzi syndrome.

Histopathological examination of the excised gallbladder showed chronic cholecystitis with extensive fibrosis and xanthogranulomatous inflammation. No evidence of carcinoma was found. The findings confirmed Mirizzi syndrome (type-I), where the impacted stone in the gallbladder neck caused extrinsic compression of the bile duct, mimicking carcinoma on imaging.

The patient recovered uneventfully and was discharged on postoperative day seven. At his follow-up appointment, jaundice had resolved, and liver function tests had returned to normal. No complications were noted, and the patient remained asymptomatic.

DISCUSSION

Gallbladder wall thickening is often an alarming finding, as it is frequently associated with malignant conditions such as gallbladder carcinoma, an aggressive cancer with poor prognosis. However, a variety of benign conditions can present with similar imaging features, leading to diagnostic confusion. This case series highlights five instances where patients presented with symptoms, imaging findings, and clinical histories suggestive of gallbladder carcinoma, but post-surgical histopathology revealed benign conditions such as xanthogranulomatous cholecystitis (XGC), porcelain gallbladder, chronic cholecystitis, and Mirizzi syndrome.

In the present study of Xanthogranulomatous Cholecystitis (XGC), for instance, the diffuse thickening of the gallbladder wall on USG and CECT abdomen closely resemble the appearance of gallbladder carcinoma on imaging. Similar to our case, Reghunath A et al (2020),[4] have discussed that XGC can be indistinguishable from carcinoma both clinically and radiologically, while histologically, XGC is characterized by extensive infiltration by foamy macrophages, multinucleated giant cells, and chronic inflammatory cells, as observed in our first case also. Although the exact etiology remains unclear, chronic inflammation from gallstones or bile stasis is thought to play a significant role as stated by Suzuki H et al (2015).[5] In this series, open cholecystectomy revealed that the suspected malignancy was, in fact, XGC, underscoring the importance of intraoperative

vigilance and comprehensive histopathological examination.

The case of Porcelain Gallbladder in our study presented a unique diagnostic challenge. The extensive calcification of the gallbladder wall, combined with chronic inflammation and cholelithiasis, closely mimicked gallbladder carcinoma on imaging. This finding, where calcifications obscure the surrounding tissues, bears a resemblance to a case reported by Goel A et al (2017),[6] which similarly demonstrated extensive gallbladder wall calcification leading to a preoperative suspicion of malignancy. While porcelain gallbladder has been associated with an increased risk of malignancy, as discussed by Karki S et al (2022),[7] our case diverges slightly from their findings. In our study, the patient was a 46-year-old female, whereas the case reported by Karki S et al (2022),[7] involved a 55-year-old female. Furthermore, we performed an open cholecystectomy due to the dense calcifications and challenging anatomy, whereas Karki S et al (2022),[7] successfully managed their case laparoscopically. Despite these procedural differences, our final histopathological analysis, like theirs, revealed chronic inflammation with dystrophic calcifications, confirming a benign condition.

Mirizzi Syndrome, featured in one of the cases, adds another layer of complexity to the diagnostic dilemma. This rare condition, characterized by the impaction of a gallstone in the neck of the gallbladder or cystic duct, can cause compression of the common hepatic duct, leading to obstructive jaundice. The clinical presentation, imaging features, and laboratory findings often mimic gallbladder carcinoma, particularly when patients present with jaundice, weight loss, and biliary dilatation. Similar findings were reported by Grohol B et al (2023),[8] and Khokhar I et al (2022).[9] In this case, preoperative imaging suggested a malignant obstruction, but the operative findings revealed an impacted stone, and histopathology confirmed benign chronic cholecystitis with fibrosis. This case highlights the importance of considering Mirizzi syndrome as a differential diagnosis in patients with obstructive jaundice and suspected malignancy.

The case of cholelithiasis with chronic cholecystitis presented a challenging diagnostic scenario. The irregular thickening of the gallbladder wall, along with chronic inflammation, raised a significant suspicion for malignancy. Obesity and long-term use of hormonal therapy, such as oral contraceptives, have been associated with an increased risk of gallbladder disease, as discussed by Etminan M et al (2011).[10] Despite the alarming imaging findings suggestive of carcinoma, the histopathological examination revealed chronic cholecystitis with multiple cholesterol stones and no evidence of malignancy.

In all five cases, the definitive diagnosis of benign conditions was only made after surgical intervention and histopathological evaluation.

Histopathology remains the gold standard for differentiating benign from malignant gallbladder conditions. In the cases presented, histological examination revealed the presence of chronic inflammatory infiltrates, fibrosis, and calcification, without any evidence of malignant cells. These findings are characteristic of chronic cholecystitis, XGC, porcelain gallbladder, and Mirizzi syndrome, reinforcing the need for surgical excision in cases of diagnostic uncertainty.[6-10]

While elective cholecystectomy remains the definitive treatment for chronic inflammatory gallbladder conditions, the approach to surgery must be tailored to the individual case, particularly in patients with severe fibrosis or complex anatomy.[6-10]

CONCLUSION

This case series highlights the diagnostic challenges posed by gallbladder wall thickening, a common radiological finding that can mimic carcinoma. Chronic inflammatory conditions such as XGC, porcelain gallbladder, and Mirizzi syndrome can present with clinical and imaging features highly suggestive of malignancy, but histopathology often reveals benign pathology. These cases underscore the critical role of surgery and histopathological examination in distinguishing benign from malignant conditions. Careful preoperative assessment, coupled with a high index of suspicion for benign disease, can prevent overtreatment and ensure optimal patient outcomes.

Informed Consent: Written informed consent was obtained from patients who participated in this case series.

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