

## Case Report

# Early gallbladder carcinoma with cholelithiasis: a rare case report

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### ABSTRACT

Gall bladder carcinoma is an exceedingly rare and fatal cancer with a high mortality rate. Detecting gall bladder carcinoma in early stages can be difficult, despite improvements in ultrasound and computed tomography (CT) imaging. Most diagnoses of gallbladder carcinoma are made at advanced stages, with majority being found incidentally during surgery for cholelithiasis. The presented case demonstrates suspicion of Gallbladder carcinoma pre-operatively.

**Keywords:** Cholelithiasis, Cholecystectomy, Extended lymphadenectomy, Gallbladder, Gallbladder carcinoma

## INTRODUCTION

Gall bladder carcinoma is an exceedingly rare malignancy in the developed world. Globally, incidence rates vary widely reaching very high rates in north and South American women. The incidence of gallbladder carcinoma in the united states is 1 to 2.5 per 1,00,000.<sup>1</sup> Due to its early vague symptoms and the gallbladder's lack of serosa to slow its spread, gallbladder carcinoma typically presents at advanced stages and carries a 5-year survival rate of less than 5%.<sup>1,2</sup>

The majority of gallbladder carcinomas are diagnosed incidentally, usually when exploring for cholelithiasis.<sup>3</sup> Several risk factors have been identified for gallbladder carcinoma. The leading risk factors include female gender, cholelithiasis and advancing age. Gallbladder polyps, porcelain gallbladder, congenital biliary cysts, abnormal pancreatico - biliary duct junction, and exposure to carcinogens have all been associated with gallbladder carcinoma.

Additional reported risk factors include smoking, obesity, diabetes, chronic infections (*Salmonella*, *Helicobacter*),

and medications such as methyldopa, ocp, isoniazid, and estrogen.<sup>4-6</sup>

Here study present a rare case of an early gallbladder carcinoma with node - negative disease found during open cholecystectomy for calculous cholecystitis.

## CASE REPORT

A 65-year-old female presented with complaints of right upper quadrant pain with low grade fever for 2 days and history of dyspepsia for 6 months duration. On examination, she had right upper quadrant tenderness, no rebound tenderness and no murphy's sign. The patient's initial blood investigations revealed mild elevation in PT, INR; otherwise, all other lab results were normal. Upper GI endoscopy revealed antral gastritis. Additionally, an ultrasound whole abdomen was performed which demonstrated lobulated heterogenous polypoidal lesion in the anterior wall of gallbladder with size of 1.5 X 1.5 cms with increased vascularity, and few mobile calculi, with largest measuring 3 mm in size. Then, CECT (contrast enhanced computed tomography) of abdomen was done, which revealed, distended gallbladder with lobulated soft tissue density mass of size 2.0 X 1.2 cm seen in the

frontal region extending into the lumen with few specks of calcifications within and 3 mm radio dense calculus noted in the neck of the gallbladder, pericholecystic fat planes were normal (Figure 1).



**Figure 1: CECT abdomen of distended gallbladder with lobulated soft tissue density mass with calculus in neck of the gallbladder.**

In view of these findings, patient was suspected for gallbladder carcinoma, and subsequently CA 19-9 was done, which showed elevated levels of 62.50  $\mu\text{ml}$ . (Normal range is  $<30.90 \mu\text{ml}$ ).



**Figure 2: Gallbladder specimen.**

All these findings raised high suspicion of gallbladder malignancy. Patient was taken to surgery for an open cholecystectomy. During the operation, patient was given 2cms clearance of liver bed margin, and specimen was sent for frozen section (Figure 2).

Frozen section of the specimen demonstrated infiltrating adenocarcinoma invading the muscularis layer.

In view of these findings, during surgery extended lymphadenectomy was done. Periportal, choledochal, retropancreatic, common hepatic, paraceliac lymphnodes along with falciform ligament was removed, and sent for histopathological examination.

The pathology revealed adenocarcinoma of body of the Gallbladder invading the muscular layer with negative margins. All nodes (0/12) were negative for adeno carcinoma, with cholelithiasis. The patient's stage of disease was determined to be PT1 b No. Her postoperative period was uneventful and recovered well. She is on regular follow-up.

## DISCUSSION

A gallbladder carcinoma is a very rare malignancy with high mortality as previously mentioned. In areas with highest incidence, like India and Pakistan, common risk factor is chronic gallbladder wall inflammation with subsequent cellular proliferation. The most common source of this inflammation is large gallstones greater than 3 cm or chronic salmonella typhi infection.

Although 75 - 90% of gallbladder cancers had a history of gallstones, only 0.3 to 3% cholecystectomies done for presumed benign gallstones showed gallbladder cancer.<sup>7,8</sup> Most gallbladder carcinoma is associated with high rate of regional lymph node metastasis and mortality.<sup>2,9,10</sup> Adjuvant chemoradiation is commonly recommended for node-positive or incompletely resected disease.<sup>11,12</sup> Therefore, early detection is important because patients found at stage T1 No would have a greater chance for surgical cure and spare them the potential toxicity of adjuvant therapy.

Early diagnosis can be difficult because symptoms can mimic or be caused by co existing cholecystitis, which is a common condition.<sup>6</sup> Therefore, screening patients who present with these symptoms is essential given the possibility for a coexisting gallbladder carcinoma. Symptoms early in the disease process can be vague, often leading to a delay in diagnosis. The most common complaint in the symptomatic patient with GBC is right upper quadrant pain, specifically in the right hypochondrium. Other warning signs, which our patient did not exhibit, include weight loss, anorexia, nausea or vomiting, jaundice, and pruritus.<sup>13,14</sup>

Routine laboratory tests are generally non-diagnostic and do not significantly improve the identification of

gallbladder carcinoma preoperatively.<sup>14</sup> Serum tumor markers, carcinoembryonic antigen (CEA), and carbohydrate antigen 19-9 (CA 19-9) are frequently elevated in patients with Gallbladder Carcinoma.<sup>15,16</sup>

Imaging with ultrasound and CT has improved preoperative diagnosis of gallbladder cancer. Despite these advancements, only 50% of Gallbladder cancers are recognized before surgery.<sup>14</sup> Ultrasound is often the initial imaging study of choice for patients presenting with symptoms consistent with gall stone disease. Ultrasound images from a group of patients diagnosed with gallbladder carcinoma incidentally were reviewed retrospectively and found to have suspicious findings on reevaluation.<sup>17</sup> The most common ultrasound findings include calcified and echogenic mucosal masses, which can be associated with cholelithiasis or porcelain Gallbladder.<sup>17</sup> High-risk features on ultrasonography also include solitary or displaced gallstone, intraluminal mass, and discontinuity of the mucosal echo.<sup>17</sup> Other findings that are suggestive of gallbladder carcinoma include the loss of the interface between the gallbladder and liver or direct liver infiltration.<sup>17</sup> Moreover, ultrasound abnormalities are often more subtle in early stage disease, making detection more challenging.<sup>17</sup> If abnormalities or suspicious findings are detected on ultrasound, further evaluation with other non-invasive imaging is warranted. Consideration of gallbladder carcinoma in the differential diagnosis may help to improve detection before surgery, potentially leading to the discovery of the disease in its early stages.

The most useful, non-invasive imaging studies for evaluating Gallbladder Carcinoma preoperatively include CT, magnetic resonance imaging (MRI). CT has been shown to be useful in defining the extent of gallbladder carcinoma and in determining the respectability in advanced stages.<sup>18,19</sup> Additionally, CT has a low to moderate sensitivity for detecting gastrointestinal, omental and abdominal wall involvement, but because of its high positive predictive value in detecting liver invasion, lymph node involvement and distant metastases, it remains a useful imaging study in gallbladder carcinoma preoperatively.<sup>18,19</sup> MRI and MRCP (magnetic resonance cholangiopancreatography) have also been shown to be useful in preoperative staging of gallbladder carcinoma with a high sensitivity in identifying hepatic invasion and lymph node metastasis.<sup>20</sup> Biopsies of the detected gallbladder masses are often performed via ultrasound guidance, CT guidance, endoscopic ultrasound guidance, endoscopic retrograde cholangiopancreatography (ERCP), or by laparoscopy.

Regarding further procedures and tests for gallbladder carcinoma, endoscopic ultrasound (EUS) is a minimally invasive procedure that has been shown to be accurate at imaging the gallbladder. Endoscopic ultrasound also helpful in the differential diagnosis of Gallbladder polyps and excellent in staging tumor depth.<sup>21,22</sup> ERCP and PET

are two less commonly used imaging modalities used for evaluating gallbladder carcinoma preoperatively.

## CONCLUSION

The presentation of gallbladder carcinoma may be very difficult to distinguish from benign pathologies like cholecystitis. The most important underlying risk factors for gallbladder carcinoma are cholelithiasis and female gender. Imaging via ultrasound and CT Scan as well as sending all gallbladders for pathology postoperatively seem to be the best ways to distinguish patients with benign disease from those with malignancy.

Our patient was female over 65 years of age with calculous cholecystitis illustrates the challenge of preoperative early-stage gallbladder carcinoma diagnosis. Early detection is important in decreasing both morbidity and mortality of gallbladder carcinoma, with potential for surgical cure in cases limited to the gallbladder. Patients with ultrasound findings such as gallstones or polyps should be offered surgical consultation. Further, consideration of gallbladder carcinoma within the differential diagnosis by surgeons, and radiologists may serve to maximize discovery before the time of surgery.

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