

## Incidental gall bladder cancer with port site metastasis; Case management in low resource setting: Case report

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### Abstract

Incidental gall bladder cancer following laparoscopic cholecystectomy for presumed benign gall bladder disease is on rise so is the incidence of port site metastasis. Herein we retrospectively reviewed the clinico-pathological profile of our patient with symptomatic gall stone disease subsequently diagnosed with incidental gall bladder cancer. The review was used retrospectively to individualize the management and discuss the loopholes encountered during the course of treatment. Evidence based yet contextual approach should be used to individualize management of incidental gall bladder cancer in low resource setting. The clinical dictum of port site metastasis as systemic spread in incidental gall bladder has to be borne in mind by the treating physician.

### Keywords

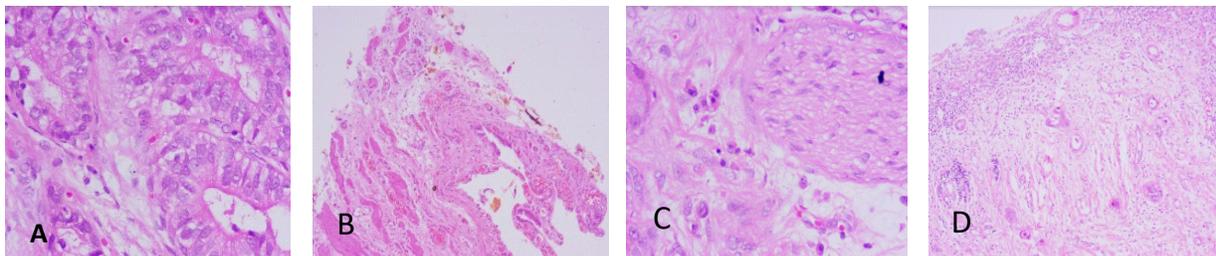
Incidental gall bladder cancer; port site metastasis.

### Introduction

Laparoscopic cholecystectomy is the commonest procedure performed worldwide for presumed benign gall bladder disease. However the postoperative histopathological diagnosis of incidental gall bladder cancer (IGBC) is on rise. IGBC following laparoscopic or open cholecystectomy is not very rare at the rate of 0.36% ranging from 0.19-1.6% [1]. Cholelithiasis leading to chronic cholecystitis has been found to be the most important risk factor in carcinogenesis of gall bladder cancer [2]. Port Site Metastasis (PSM) following IGBC is found in 16% of the cases [3]. Various mechanisms have been proposed for its occurrence. Some of the mechanisms reported are the more biologically aggressive tumor, manipulation of gall bladder causing perforation and spillage, unbagged specimen during extraction and pneumoperitoneum factors leading to contamination of the port sites [4].

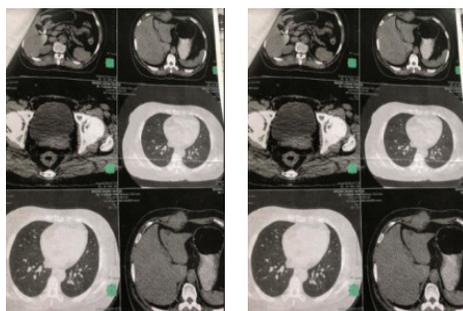
## Case Presentation

This is a P2-0-0-2 50 years old postmenopausal women who underwent laparoscopic cholecystectomy in 2017 for symptomatic gall stone disease. The intraoperative and postoperative period were uneventful. Examination of the gall bladder showed focal thickening over the fundus measuring 1.5 centimeters. The histopathology result of the specimen showed well differentiated adenocarcinoma of the gall bladder with negative surgical margins but involving the perimuscular tissues (Figure 1). The tumor was found more towards the hepatic side. A retrospective diagnosis of gall bladder adenocarcinoma T2b was made as per the AJCC manual, 8th edition. Postoperative CECT abdomen assessment did not reveal any loco-regional residual disease or distant metastasis.

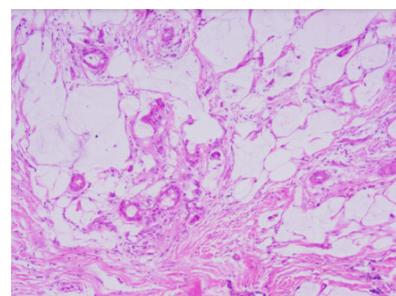


**Figure 1:** Microscopic image showing (A) adenocarcinoma of gall bladder (B) resection margin (C) absent perineural invasion D) serosal surface

However, the patient developed mild epigastric pain at 6 months of surgery. She noticed a tender lump over the epigastrium which gradually increased. Initial examination at the surgical OPD revealed a hard mass at the epigastric port site. CECT whole abdomen showed no significant abnormalities except for the irregular soft tissue mass of 4.9 X 3 cm in the right rectus abdominis muscle projecting into the subcutaneous tissues (Figure 2). Tumor markers Ca19-9 and CEA were within normal limits. Wide surgical resection was performed at the epigastric port site which revealed few signet ring cells and dysplastic glands suggestive of port site metastatic adenocarcinoma (Figure 3). The excised surgical margins were negative for tumor (< 1 mm). She underwent external beam radiation therapy with 50Gy divided over 25 doses. Regular follow up for one year post radiation did not reveal any significant abnormalities in ultrasonography of whole abdomen, tumor markers and liver function test.



**Figure 2:** MCECT abdomen showing soft tissue mass in anterior abdominal wall.



**Figure 3:** Adenocarcinoma of epigastric soft tissue mass

However, she complained of palpable lower abdominal mass which was growing rapidly over the next 6 months. Examination revealed a 10 x 10 centimeter, firm to solid, non tender, nodular abdominopelvic mass. There was no hepatosplenomegaly or ascites. Ultrasound showed multi septate cystic lesion in pelvis 11.6 x 15 centimeters. Tumors markers were within the normal range.

Exploratory laparotomy showed bilateral ovarian mass (left>right) with smooth but nodular surface measuring 19 x 12 centimeters and 6.5 x 4 centimeters respectively (Figure 4A). No ascites was noted. Surgical staging was carried out.

Histopathology findings were compatible with bilateral Krukenberg tumor with capsular involvement (Figure 4B). Uterus, tubes, omentum and appendix were unremarkable.

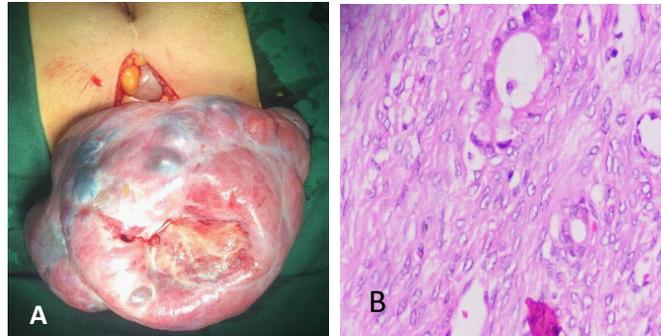


Figure 4: Krukenberg tumor (A) gross appearance (B) microscopic image

## Discussion

Clinical presentation of benign gall bladder disease and early gall bladder cancer looks similar. The clinician is swayed by the more commonly occurring stone. Nevertheless, suspicious sonographic findings of the hepatobiliary system and intraoperative findings could possibly avert the diagnosis of incidental gall bladder cancer at least in one third of the cases. Preoperative sonography showing diffuse or focal thickening of the gall bladder wall, gall bladder mass or intraoperative finding of dense adhesion were associated with gall bladder cancer in around half of the cases [1,5]. In presence of these features, the surgeon should have high degree of suspicion for malignancy and perform frozen section.

PSM is more commonly seen in  $\geq$  T2 tumor signaling occult peritoneal seeding and metastasis. Resection of the port site during re resection with curative intent therefore did not improve survival [6,7]. Using the 8<sup>th</sup> edition of AJCC manual, our case was a T2b well differentiated adenocarcinoma of gall bladder on the hepatic side without perineural or lymphovascular invasion and negative surgical margin. These histopathological parameters were reported as favorable in terms of predicting residual disease and survival [8]. The hepatic location of the tumor probably nullified the other favorable prognostic factors in terms of residual disease and locoregional recurrence [9,10].

Re-resection in our case was not performed due to free surgical margin of the gall bladder specimen and absence of visible residual disease on CECT abdomen. Presumed R0 resection at primary surgery however has to be supplemented with the more significant prognostic factor of T stage. Even well differentiated T2 IGBC has 35% probability of residual disease which is clinically significant [8]. Population based study by Yang et al has found 44% of those with T2 tumors had nodal involvement [11]. Following R0 resection with primary surgery, re-resection was associated with significant survival benefit compared to no re-resection [10]. This indirectly implies presence of residual disease in those with R0 margin achieved with primary surgery. The sensitivity of CT scan in detecting residual disease is at best 43% as reported by Shukla et al [12]. Regional lymph nodes and occult peritoneal seeding are often missed by CT scan.

The role of adjuvant therapy in terms of better overall survival has been advocated by American Society of Clinical Oncology 2019 based on BILCAP study by Primrose et al. This study had demonstrated clinically significant overall survival in adjuvant capecitabine therapy compared to observation group in those with surgery with curative intent [13]. Studies by Ma et al and T. Mitin et al has shown better overall survival with adjuvant therapy in high risk patients with R1/2 resection margin, node positivity and  $\geq$  stage T2 patients [14,15]. Simple cholecystectomy plus adjuvant therapy done at the minimum still conferred some overall survival benefit compared to simple cholecystectomy [16]. The EBRT post resection of PSM did not halt the occurrence of Krukenberg tumor implying it as a systemic rather than a locoregional recurrence.

Going retrospective, there was definite role of re resection or atleast adjuvant therapy in our case. The pitfall in optimal management of this case were multifactorial- lone surgical oncologist, no medical oncologist and tumor board. Initiating the adjuvant therapy post primary surgery would have been the better “Individualized” management. Study by LI W et all on ovarian metastasis has reported a dismal median survival of eight months [17]. They also described gastrointestinal primary, mucinous or signet type, synchronous metastasis and massive ascites were associated with poor survival. The patient has denied palliative chemotherapy.

## Conclusion

Evidence based yet contextual approach based on clinico- pathological profile on T stage, margin status of the specimen and postoperative imaging should individualize management of incidental gall bladder cancer in low resource setting. The clinical dictum of PSM as systemic metastasis should be borne in mind by the treating physician.

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