International Surgery Journal
*Thammaiah P. Int Surg J. 2022 Oct;9(10):1770-1775*
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: https://dx.doi.org/10.18203/2349-2902.isj20222606

**Case Report**

# Extended radical cholecystectomy with curative potential for well selected locally advanced carcinoma gall bladder: a case report and review of literature

**Pradeep Thammaiah***

Department of Surgical Oncology, Santhiram Medical College, Nandyal, Andra Pradesh, India

**Received:** 28 July 2022
**Accepted:** 26 August 2022

***Correspondence:**
Dr. Pradeep Thammaiah,
E-mail: dr.pradyrt58@gmail.com



## ABSTRACT

Gallbladder cancer is an aggressive malignancy that is associated with a poor prognosis. While surgical resection provides the only curative option, the majority of patients are not considered resectable due to locally advanced disease and presence of metastatic disease at the time of presentation. Here we presented a case of 46-year-old female with symptoms and initial workup suggestive of obstructive jaundice with cholestasis. PET-CT demonstrated heterogeneously enhancing mass lesion arising from neck of gallbladder and involving adjacent liver parenchyma with FDG avid para-aortic nodes. Liver biopsy confirmed adenocarcinoma, ERCP revealed tight hilar structure and CBD stent was placed. Patient was diagnosed with cT4, N2 carcinoma gall bladder and received two cycles of neoadjuvant chemotherapy (NACT) with gemcitabine and cisplatin. In view of localized and stable disease following NACT, patient underwent radical cholecystectomy with wide liver resection involving segment 4b and 5 with hepatoduodenal, portocaval and aortocaval lymph node dissection. Patient had post-operative complications, managed conservatively. On follow up patient had improved appetite, gained weight adequately, received adjuvant chemotherapy and is disease free till date. Carefully selected patients may benefit from an aggressive surgical approach following upfront systemic chemotherapy.

**Keywords:** Carcinoma gall bladder, Locally advanced, Neoadjuvant chemotherapy, Adjuvant therapy, R0 resection, Survival

## INTRODUCTION

Gall bladder cancer ranks sixth among the gastrointestinal malignancy and most common biliary tract cancer.[1] The incidence of gall bladder cancer varies widely; it is less common in majority of world with worldwide incidence of less than 2.2/100000 in male and 2.4/100000 in females.

Countries with highest incidence adjusted for age in females per 100000 are Bolivia (15.1), Chile (11.7), Bangladesh (7.3), Nepal (7.3) and Peru (6.0). The age-adjusted mortality rate being 1.6 per 100000 for male and 1.8 for female with cumulative risk of dying is 0.17% and 0.19% respectively.[2]

Despite advances in diagnostic modalities, due to nonspecific symptoms, anatomical position of gall bladder most patients present to the clinician at an advanced stage when the outcome is very poor, and the overall 5 year survival rate is less than 5%.[3]

Radical surgical resection has been only effective way offering curative treatment to increase five year survival in patients with ca gall bladder.[4] Thus, extensive surgery including extended hepatectomy, pancreaticoduodenectomy with lymph node dissection should be considered when RO resection is feasible and have shown curative potential.

In this paper we presented management of a case of locally advanced gall bladder carcinoma (LA CAGB) and the review of literature for the management of non-metastatic locally advanced carcinoma gall bladder.

## CASE REPORT

Our patient was a 46 years female, presented with h/o nausea, yellowish discoloration of eye, loss of weight and appetite, all for 15 days, associated with itching and clay coloured stool, no fever, no melena, no waxing and waning of jaundice, features s/o obstructive jaundice.

Patient was evaluated for above complaints, investigations: Hb- 10.4, T.bilirubin- 9.1, direct-8, alkaline phosphatase- 497, SGPT/SGOT- 158/105, CEA- 19.47, calcium- 19-9-821.2 s/o obstructive jaundice with cholestasis.

PET-CT-FDG avid (SuvMax 20.1) heterogeneously enhancing soft tissue lesion from the neck of gall bladder extending into the hepatic hilum involving cystic and common hepatic ducts.

FDG avid heterogeneously enhancing mural thickening in body and fundus of gall bladder along the postero-lateral wall with loss of fat plane with segment 4b and 5 of liver s/o infiltration. Lesion is seen to abut pylorus, duodenum and hepatic flexure with loss of fat plane. FDG avid gastrohepatic (Suv max-4.6), aortocaval, paraortic and portocaval nodes noted

Biopsy from liver-adenocarcinoma, Ercp done showed tight hilar stricture, 10 FR 10 cm CBD stent was placed. Post stenting bilirubin decreased- T. bilirubin- 2.2, direct-2.

Diagnosed with carcinoma gall bladder with clinical stage-T4 N2.

Treatment options in this otherwise young patient with good performance status with clinically locally advanced non-metastatic ca gall bladder- galliative chemotherapy, upfront surgery followed by chemotherapy, best supportive care, and neoadjuvant chemotherapy (NACT) followed by surgery. In view of LA CAGB patient was planned for NACT.[5-7] Received 2 NACT with gemcitabine and cisplatin.

Post-NACT evaluation, PET CT- compared to previous PET CT there was mild decrease in metabolic activity of lesion and nodes however there was minimal increase in the extent of primary disease.

Triphasic CT- heterogeneously enhancing soft tissue mass involving gall bladder, contiguously infiltrating into segment 5 of liver with associated pericholecystic fat stranding and thickened right gerota fascia. Lesion involves hepatic hilum encasing the stented common hepatic and bile duct abutting the common and right hepatic artery causing no obvious luminal narrowing and also abutting the main portal vein at the hilum.

Mass also abuts the adjoining hepatic flexure, pylorus and the first part of the duodenum with effaced fat planes. Focal discontinuity of the right lateral wall of first part of duodenum also noted with extravasation of oral contrast and air locules in the mass. Few periportal, peripancreatic, portocaval, aortocaval, gastrohepatic, pre and para aortic nodes are persistently noted, no ascites.

In view of, nearly stable disease after NACT, young age with good performance status, and localised disease. Patient and the relatives were motivated, decided for aggressive surgical approach.

## CASE REPORT

### *Surgical management*

Diagnostic laparoscopy was done- no peritoneal deposits were found. Explored with chevron incision, Kocherisation done to access the aortocaval nodes, multiple enlarged aortocaval nodes dissected and sent for frozen section- reports were negative for metastasis, proceeded with definitive surgery

### *Findings*

The findings were as follows- (1) large mass involving gall bladder body and neck extending contiguously into liver in GB bed, pylorus and 1st part and initial 2nd part of duodenum, calots frozen and extending just upto hilum of bile duct; (2) right hepatic artery passing through the tumor mass; (3) portal vein free; (4) no peritoneal deposits; (5) no ascites; (6) multiple enlarged aortocaval and hepatoduodenal nodes.

### *Surgery*

Underwent radical cholecystectomy with wide anatomical liver resection segment 4b and 5, resection of pylorus, first and initial second part of duodenum. Hepatoduodenal, portocaval and aortocaval nodes dissected. Right hepatic artery ligated (involved by disease). CHD transected at the hilum. Anastomosis-Roux-en-Y, roux limb- hepatico-jejunostomy, Y limb- gastrojejunostomy and jejuno-jejunostomy. Naso-Jjejunostomy tube for feeding was inserted.

### *Histopathology reports*

Moderately differentiated adenocarcinoma of gall bladder, tumor invades entire thickness of the gall bladder wall to involve the liver, common bile duct and duodenum. Perineural invasion and lymphovascular invasion are seen. Proximal CBD margin show focal high-grade dysplasia, Revised CBD cut margin- free of tumor. Rest cut margins are free. Aotocaval nodes 0/3 positive, hepatoduodenal

nodes 0/3 positive and superior pancreatic nodal mass free of tumor.

***Post-operatively***

Patient was managed in intensive care unit, started on NJ feeds on POD-2. Patient had persistent tachycardia, tachypnea and intermittent fever.

Bilateral pleural effusion was diagnosed, tapping was done. Transient depressed liver function recovered over time.

CT done in post-op period showed anastomotic site normal, ill defined non-enhancing hypodense areas seen involving segment 6 and minimally of segment 7 s/o ischemia, multiple discrete as well as branching air foci seen within this area s/o infection. Fluid aspirated from this site showed growth of enterococcus fecalis, wound swab growth of klebsiella and Urine culture- growth of candida.

Managed with appropriate antibiotics according to culture sensitivity. Patient had continuous purulent discharge from the drain site, stopped over a period of one and half month.

Follow up CT scan dated (Figure 3) showed heterogenous enhancement in segment 6 of right lobe of liver, small residual collection.

Received adjuvant chemotherapy. Patient in remission till date.

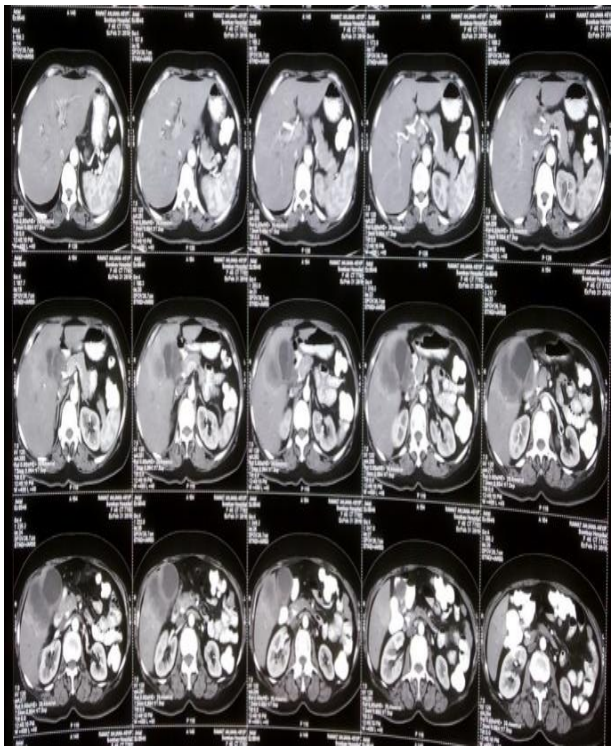

**Figure 1: Pre-operative CECT (A+P) showing enhancing mass lesion of GB with contiguous involvement of liver.**

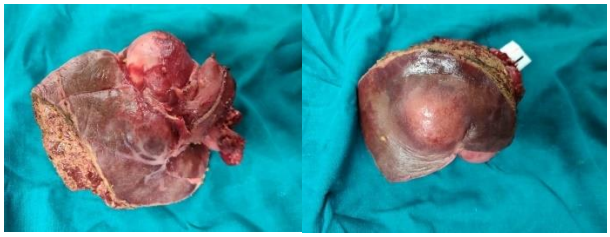

**Figure 2: Images of gross specimen.**

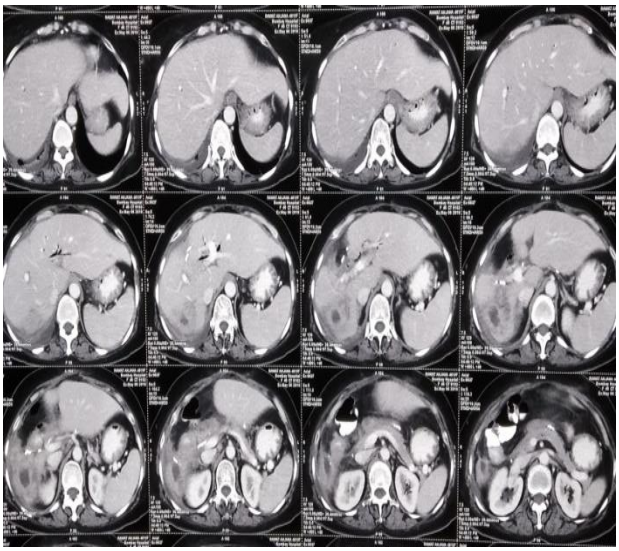

**Figure 3: Post-operative images showing near complete resolution of ischemic and necrotic segment 6 and 7.**

## DISCUSSION

***Review of literature- management of advanced carcinoma gall bladder***

Alfred Blalock wrote in 1924 that *"in malignancy of the gallbladder when a diagnosis can be made without exploration, no operation should be performed, in as much as it only shortens the patient's life"*. This pessimistic view of gallbladder cancer is understandable because, this rapidly growing tumor has a propensity for early dissemination. Furthermore, the gallbladder is in close proximity to liver, other visceral organs and major vasculature requiring extensive hepatic, other adjacent organ resections and vascular reconstruction are to eradicate local disease.[8] Also confirmed by a review of 6222 cases in 1978 showed an overall 5 year survival of 4.1 % with a median survival of 5 to 8 months.[9] Even after a decade the same poor survival rate had been observed, 5% and 12% 5-year survival from France and Australia.[10,11] However, in the recent years with the improved surgical technique and more extensive resection a better survival has been achieved as shown by a Canadian study in 2005 wherein an overall 5 year survival of 35% was seen in the second half of study period.[12] In a retrospective study by Kondo at al 68 patients were identified with stage 3 and stage 4 disease underwent

extensive resection including extended right hepatectomy, pancreaticoduodenectomy, and/or portal vein resection.[13]

Of these 13 had survived for >3 years and 9 >5 years, no significant statistical difference between survival rates for stage 3 (44% at 3 years, 33% at 5 years) and stage 4 (M0) (24 % at 3 years and 17 % at 5 years) was observed but it was better than patients with stage 4 (M1) disease p=0.009 and p=0.062 respectively. Post-op mortality observed were all in patients with extended right hepatectomy who died of liver failure.

Also, patients with limited distant metastasis underwent resection but with dismal advantage. They concluded that there were significant survival benefits for a locally advanced disease where extensive resection can be done to achieve a R0 resection, but somewhat of limited value if requires pancreaticoduodenectomy or portal vein resection. In another retrospective study by Birbaum et al where they investigated the role of major adjacent organ resection on survival in locally advanced (cT3-T4) ca gall bladder, 78 patients had undergone major resection and 86% achieved R0 resection.[14] Only patients with R0 resection showed survival benefits with 26% 5-year survival in later part of study from 2003 to 2011. Patients undergoing major adjacent organ resection including pancreaticoduodenectomy and colectomy or gastrectomy fared poorly with 0% survival at 2 year and 3 year respectively even after achieving R0 resection raising an apprehension on the survival advantage of surgery. CBD resection and major hepatectomy did not affect the outcome. They also made the following observation that presence of paraaortic nodes was not a contraindication for surgery, N1 and N2 disease had similar outcome and perineural infiltration was another strong prognostic factor.

In a study by Nishio et al 100 patients with locally advanced ca gall bladder underwent hepatectomy and bile duct resection with or without adjacent organ resection.[15] Sixty-one patients had major adjacent organ resection other than liver and bile duct. The 5-year survival rate and median survival without combined resection of adjacent organ (CRAO) is 36% and 3.8 years and with CRAO is 16% and 0.8 years respectively. Thus, suggesting locally advanced ca gall bladder extending onto extrahepatic bile duct requiring extensive resection including hepatectomy without CRAO, when R0 resection can be achieved can have a better 5-year survival while the same was not true when CRAO was required.

Gemcitabine with cisplatin became the standard of care for adjuvant therapy in gall bladder- ABC 02 trial.[16] But the benefit of NACT in ca gall bladder has conflicting results with increasing resectability and survival while raising concern regarding surgical delay and disease progression. Most studies of locally advanced ca gall bladder with resection after NACT have shown that patients who achieve R0 resection after NACT are the one with survival advantage.[5-7,17]

In a study by Creasy et al 22 among 74 patients attempted surgery after NACT who showed stable disease or partial response.[6] Ten of 22 achieved R0 resection and had a significant median survival of 54 months. Similar results have been shown by Chaudhari et al with a median survival of 49 months and recurrence free survival of 25 months after R0 resection.[7]

**Table 1: Showing various case series with aggressive surgical management for locally advanced ca GB.**

| S. no | Author | Year | No of patients | Neo-adjuvant chemotherapy | Procedures performed with radical cholecystectomy | Resection rate (%) | Post op mortality (%) | Post-op morbidity (%) | Median overall survival (months) | 5 year survival (%) | Recurrence free survival (month) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **1** | Yuman et al | 2000 | 102 | No | Right trisegmentectomy, left trisegmentectopmy, right lobectomy CBD resection | NA | 4 | 29 | 26 | 21 for T3<br>28 for T4 | NA |
| **2** | Kondo et al[13] | 2002 | 68 | No | Extended right hepatectomy, Pancreaticoduodenectomy, portal vain resection | 65 | 18 | 51 | NA | 33% for st 3 and 17% for st 4 | NA |
| **3** | Nishio et al[15] | 2011 | 100 | No | Hepatectomy and bile duct resection with or without combined resection of adjacent organs (CRAO) | NA | 9 | 61 | 44 without CRAO, 9 with CRAO | 16 for CRAO<br>36 without CRAO | NA |

Continued.

| S. no | Author | Year | No of patients | Neo-adjuvant chemotherapy | Procedures performed with radical cholecystectomy | Resection rate (%) | Post op mortality (%) | Post-op morbidity (%) | Median overall survival (months) | 5 year survival (%) | Recurrence free survival (month) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **4** | Birbaum et al[14] | 2014 | 78 | no | Pancreaticoduodenectomy, extended liver resection, gastrectomy, right colectomy, CBD resection | 86 | 8 | 47 | 16 | 9 before 2003<br>26 from 200320<br>11 | 10 |
| **5** | Sirohi et al[17] | 2015 | 37 | yes | Hepatectomy, partial colectomy, partial duodenectomy | 45.9 | NA | NA | 40.9 | NA | 25.9 |
| **6** | Creasy et al[6] | 2017 | 74 / 10 pts achieved R0 resection | yes | Extended hepatectomy, Pancreaticoduodenectomy, partial duodenectomy | 13.5 | | | 51 | | |
| **7** | Chaudhari et al[7] | 2018 | 160 | Yes | Radical cholecystectomy Bile duct excision Combined adjacent organ resection (CRAO) | 63 pts 39.3 | 1.1 | 12.9 | 49 | | 25 |

## CONCLUSION

Careful selection of patients is the key in managing locally advanced ca GB. Aggressive surgical approach including adjacent organ resection to achieve a R0 resection following neo-adjuvant chemotherapy can improve long term outcome in LA CAGB.

*Funding: No funding sources*
*Conflict of interest: None declared*
*Ethical approval: Not required*

## REFERENCES

1. Mahdavifar N, Mohammadian M, Salehiniya H. Gall bladder cancer in the world: Epidemiology, incidence, mortality and risk factors. World Cancer Res J. 2018;5(3):e1124.
2. Ferlay J, Colombet M, Soerjomataram I, Mathers C, Parkin DM, Piñeros M, et al. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. Int J Cancer. 2019;144(8):1941-53.
3. Goetze TO. Gallbladder carcinoma: Prognostic factors and therapeutic options. World J Gastroenterol. 2015;21(43):12211-7.
4. Misra S, Chaturvedi A, Misra NC, Sharma ID. Carcinoma of the gallbladder. Lancet Oncol. 2003;4(3):167-76.
5. Engineer R, Goel M, Chopra S, Patil P, Purandare N, Rangarajan V, et al. Neoadjuvant Chemoradiation Followed by Surgery for Locally Advanced Gallbladder Cancers: A New Paradigm. Ann Surg Oncol. 2016;23(9):3009-15.
6. Creasy JM, Goldman DA, Dudeja V, Lowery MA, Cercek A, Balachandran VP, et al. Systemic Chemotherapy Combined with Resection for Locally Advanced Gallbladder Carcinoma: Surgical and Survival Outcomes. J Am Coll Surg. 2017;224(5):906-16.
7. Chaudhari VA, Ostwal V, Patkar S, Sahu A, Toshniwal A, Ramaswamy A, et al. Outcome of neoadjuvant chemotherapy in "locally advanced/borderline resectable" gallbladder cancer: the need to define indications. HPB (Oxford). 2018;20(9):841-7.
8. Fong Y, Jarnagin W, Blumgart LH. Gallbladder cancer: comparison of patients presenting initially for definitive operation with those presenting after prior noncurative intervention. Ann Surg. 2000;232(4):557-69.
9. Piehler JM, Crichlow RW. Primary carcinoma of the gallbladder. Surg Gynecol Obstet. 1978;147(6):929-42.
10. Cubertafond P, Gainant A, Cucchiaro G. Surgical treatment of 724 carcinomas of the gallbladder. Results of the French Surgical Association Survey. Ann Surg. 1994;219(3):275-80.
11. Wilkinson DS. Carcinoma of the gall-bladder: an experience and review of the literature. Aust N Z J Surg. 1995;65(10):724-7.
12. Dixon E, Vollmer CM, Sahajpal A, Cattral M, Grant D, Doig C, et al. An aggressive surgical approach leads to improved survival in patients with

gallbladder cancer: a 12-year study at a North American Center. Ann Surg. 2005;241(3):385-94.
13. Kondo S, Nimura Y, Hayakawa N, Kamiya J, Nagino M, Uesaka K. Extensive surgery for carcinoma of the gallbladder. Br J Surg. 2002;89(2):179-84.
14. Birnbaum DJ, Viganò L, Ferrero A, Langella S, Russolillo N, Capussotti L. Locally advanced gallbladder cancer: which patients benefit from resection? Eur J Surg Oncol. 2014;40(8):1008-15.
15. Nishio H, Ebata T, Yokoyama Y, Igami T, Sugawara G, Nagino M. Gallbladder cancer involving the extrahepatic bile duct is worthy of resection. Ann Surg. 2011;253(5):953-60.
16. Valle J, Wasan H, Palmer DH, Cunningham D, Anthoney A, Maraveyas A, et al. Cisplatin plus gemcitabine versus gemcitabine for biliary tract cancer. N Engl J Med. 2010;362(14):1273-81.
17. Sirohi B, Mitra A, Jagannath P, Singh A, Ramadvar M, Kulkarni S, Goel M, Shrikhande SV. Neoadjuvant chemotherapy in patients with locally advanced gallbladder cancer. Future Oncol. 2015;11(10):1501-9.

**Cite this article as:** Thammaiah P. Extended radical cholecystectomy with curative potential for well selected locally advanced carcinoma gall bladder: a case report and review of literature. Int Surg J 2022;9:1770-5.