

CLINICAL PROFILE AND MANAGEMENT OF GALL BLADDER CANCER: OUR EARLY EXPERIENCE

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Abstract

Objective: To evaluate the clinical profile of patients with gallbladder cancer.

Methodology: This is a single institution based retrospective study of patients with gallbladder cancer who presented at College of Medical Sciences and Teaching Hospital, Bharatpur, Chitwan, Nepal. Patients presenting during the two years period from August 2011 to July 2013 were reviewed.

Result: Out of 12 patients, 9 were females (75%) and 3 were males (25%), showing female preponderance. Most of the patients (75%) were in age group of 51-70 years. Only one patient (8%) was below 50 years of age. Main symptom was pain associated with anorexia, nausea & vomiting. Major signs were palpable mass, hepatomegaly and jaundice. All the histopathological reports were adenocarcinoma. 8 patients (66.66%) presented with advanced disease and were managed with extended cholecystectomy followed by systemic chemotherapy.

Conclusions: Prevalence of gall bladder cancer is higher in females in our series. Most of the patients were in fifth to seventh decade of life and presented in advanced stage. Gallbladder cancer showed association with gallstones.

Key Words: *Gallbladder cancer, extended cholecystectomy, cholelithiasis.*

Introduction

Carcinoma of the gallbladder (GBC) is the most frequent malignant tumor of the biliary tract and the fifth most common cancer of the digestive tract. Gallbladder cancer is an aggressive malignancy and carries extremely poor prognosis. Patients commonly present in late stage as it has no disease specific presenting symptoms. Have no specific presenting symptoms and therefore presentation with late – stage disease is common. In the United States and European countries, GBC is an uncommon tumor accounting for less than 2% of all cancer reported annually. However, 6000 to 7000

new cases are reported annually in the United States. Ethnicity plays an important role in the development of GBC with highest incidence in the women population from India and Pakistan. Among North American populations, Native Americans and immigrants from Latin America have the highest rate. The reasons for these geographical or ethnic variations for biliary tract cancer are not clear, but some unknown environmental risk factors or a genetic susceptibility are suspected. Most of the patients reported are female over 50 years of age and with concomitant gall stone. Presence of gallbladder stone is considered as the primary risk factor and larger stone (>3cm)

carry an increased risk of cancer development. It is 7 times more common in patients with cholelithiasis. The risk of gallbladder cancer increases with certain risk factors like abnormal pancreaticobiliary junction (APBJ), choledochal cyst, primary sclerosing cholangitis (PSC), porcelain gallbladder and GB polyps larger than 10 mm.

Other factors that are associated with GBC are pregnancy, female sex hormones, low fiber, vitamin A intake and high fat intake. There may be an association between chronic typhoid infections and subsequent development of gallbladder cancer and the likelihood of such a progression is six times higher than in normal subjects. The commonest histological type is adenocarcinoma. This may be glandular, medullary, scirrhous, papillary or colloid. It appears that papillary forms have a better prognosis than the nodular infiltrate form. Occasionally, undifferentiated carcinoma, squamous cell carcinoma, carcinoma in situ and a mixed group of rarities are reported. Very rarely, malignancy may develop from non-papillary adenomas, especially large ones over one centimeter in diameter.

The purpose of conducting this study was to evaluate the clinical profile of patients presenting to us and subsequently diagnosed with GBC.

Methodology

Patient and Study design

This is a retrospective study conducted at College of Medical Science and Teaching Hospital (COMS-TH), Bharatpur, Nepal after the approval from the ethical committee. Data were collected from the OT register and medical record files. There were total 12 cases of GBC admitted in between August 2011 and July 2013. Each patient's record was examined carefully to obtain the following data: age, sex, duration of symptom, presenting symptoms and signs, type of

operative procedure, operative findings, presence or absence of stones in gallbladder, histopathology of the resected specimen, perioperative complications and adjunctive therapy.

Results

The mean age in the study was between 51-70 years. Nine out of the total 12 patients comprising 75 % were females and 25% (n=3) were males. Age and sex distribution of these patients is given in Table-I.

Table 1. Age and Sex distribution of study population.

Age	Male	Female	Total Percentage (%)
<50	1	1	16.66 (n= 2)
51-70	1	7	66.66 (n= 8)
>70	1	1	16.66 (n= 2)
Total	3	9	100%

Table 2. Clinical presentation

SN	Symptoms	Percentage (%)
1	Non-specific chronic abdominal pain, nausea, vomiting	58.33
2	Early satiety, abdominal fullness, anorexia	16.66
3	Jaundice	16.66
4	Weight loss, pruritus	8.33
	Total	100
	Signs	
1	Palpable RUQ mass with hepatomegaly	58.33
2	Emaciation and Cachexia	16.66
3	Ascites and peripheral edema	16.66
4	Acute cholecystitis	8.33
	Total	100

Mean duration of presentation was variable which ranged from 2 days to 10 years. Patient presenting with the features of acute cholecystitis that underwent cholecystectomy and histopathologically diagnosed as GBC was the one who presented with the shortest duration of symptom. Among the remaining cases, majority of the patients presented with the symptoms like chronic epigastric pain, nausea and vomiting comprising 58.33% (n=7) while early satiety, sense of fullness and anorexia was present in 16.66 % and 16.66% presented with jaundice. Weight loss, abdominal distention and pruritus were associated with the late stage of the disease which was observed in 8.33%. Palpable right upper quadrant mass and hepatomegaly were present in 58.33% of the patients which was the major sign in our study. Of the study population, 16.66% presented with emaciation and cachexia while ascites and peripheral edema was seen in two patients (16.66%). Remaining 8.33% presented with features of acute cholecystitis. Imaging modalities, mainly USG, revealed gallstones in 75% (n=9) and gallbladder mass in 25% (n=3). Extended cholecystectomy was performed in 5 cases and completion extended cholecystectomy was done in 1 case who had undergone open cholecystectomy for acute cholecystitis, while 6 out of the 12 cases were inoperable. Systemic chemotherapy was initiated in all of the 12 patients. The histopathology report of the 6 resected specimens confirmed adenocarcinoma of gallbladder. The rest of the patients who were designated as inoperable by CT scan of abdomen and pelvis were diagnosed to have GBC on the basis of USG guided tissue biopsy. The intra-operative findings seen in the study population is demonstrated in the Table-III. There was no significant perioperative complications noted.

Table 3. Intraoperative findings (n=6)

S.N.	Findings	Percentage (%)
1	Pericystic LN involvement.	33.33(n=2)
2	Liver metastases (including completion extended cholecystectomy)	49.99(n=3)
3	Limited to gallbladder	16.66(n=1)

LN=Lymph Node

Discussion

In our study, GBC was predominant in female with the ratio of 3:1(F:M) and is similar to the findings as reported in by Patrick G et al. Most of the patient in our study were in the age group of 51-70 years. This data is consistent with the data in different literature where it has been found that in more than 75 % of the cases of the GBC mean age was more than 65 years. Because 90% of gallbladder cancer originate in the fundus or body, they don't produce symptoms until the disease is advanced. In our series, 58.33% of population presented with nonspecific symptoms like abdominal pain, nausea and vomiting. Mirsa S et al has also mentioned that due to the nonspecific symptoms and signs, establishing a proper diagnosis is difficult in case of gallbladder carcinoma. In our series, association of gallstone with gallbladder cancer was found in 75% while Marcus CB has shown that 95% of the cases with GBC have gallstones. The histopathological report in Kyriacou E revealed adenocarcinoma of gallbladder and similar result was seen in our study too. Resection of the gallbladder cancer remains the only potential for cure. Patients are divided into four specific sub-group of presentation – patient with an incidental polyps on imaging, patient with an incidental finding of gallbladder cancer at time of or

following cholecystectomy, patients suspected of having gallbladder cancer preoperatively and patients with advanced disease at presentation. For polyp and gallbladder cancer following cholecystectomy with T1a & b, simple cholecystectomy is sufficient as long as the margins are negative. However, the perilymphatic and vascular invasion is high with the T1b stage so extended cholecystectomy directed at obtaining R0 resection with excision of draining lymph node is the treatment of choice. For T2, T3 and T4 stages, radical cholecystectomy is indicated. Debulking without possibility of complete resection has no role in the management of gallbladder cancer. When disease is too advanced, only palliative procedures are done. In our study, extended cholecystectomy was done in all the operated cases (n=6) and followed by oral gemcitabine. Most of the patients were discharged with the mean duration of hospital stay of 10 days ranging from 7 to 20 days.

Conclusion

Gallbladder is a rare entity with silent progression thus present in advanced stage carrying high rate of mortality and morbidity. It is more common in female than in male. Presence of gallstone has higher risk of malignancy. Therefore, early cholecystectomy for cholelithiasis is the best way to prevent gallbladder cancer to some extent. Different literatures suggest that overall survival of the gallbladder cancer is less than 15 % with median survival of 13 months in metastatic disease. The five year survival couldn't be commented on this study because of short

duration of follow up and the timing of study performed.

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