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ORIGINAL ARTICLE

GALL BLADDER CARCINOMA: OUR INSTITUTIONAL EXPERIENCE

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Abstract

Aim: To evaluate patients with gall bladder carcinoma to define the demographics, modes of presentations, clinical staging, pathological characters and survival.

Methods: A retrospective study on 80 patients with gall bladder carcinoma at Gastroenterology Surgical Center, Mansoura University between 1990 to 2012. There were 45 males & 35 females with an average age of 53 years. Patients were classified according to the mode of presentation into four groups and the treatment modalities were according to presentation, state of the tumor & associated liver condition. All patients were followed up by ultrasound (or CT) every 6 months postoperatively. Survival was monitored with respect to the histological type of the tumor & stage of the disease.

Results: Gall bladder carcinoma represented 1.3% of a total of 5980 cases of abdominal malignancies in our center. HCV infection was present in 15% and associated gall stones in 45% of patients. We had 40 (50%) patients with gall bladder mass or obstructed gall bladder, 23 (28.75%) with symptomatic gall stones, 15 (18.75%) with obstructive Jaundice and 2 (2.5%) with gastrointestinal bleeding. Extended cholecystectomy done in 32 (4o %) patients but nothing done for 26 (32.5%) patients due to advanced tumor . Right hepatectomy was done for 12 (15%) patients due to infiltration of right liver lobe & right hepatic duct. Laparoscopic cholecystectomy was done for 8 (10%) patients as tumour was discovered accidentally. Extended cholecystectomy plus right hemicolectomy for one patient & for the last patient extended cholecystectomy was done with pancreaticodudenectomy. Survival was from 8-43 months according to line of treatment, but 5 year- survival was zero percent.

Conclusion: Gall bladder carcinoma is not uncommon with poor prognosis. Prevention is important & routine postoperative histopathology is mandatory.

Keywords: Extended cholecystectomy, laparoscopic cholecystectomy, obstructive jaundice.

INTRODUCTION

Gall bladder carcinoma is the fifth most common gastrointestinal cancer and 1-2 % of patients who have operation for cholelithiasis are diagnosed with gall bladder carcinoma at the time of surgical exploration or at the histological examination of the resected gall bladder.[1] Gall bladder carcinoma was found on 0.1-1 % of autopsies; that is 0.2-2 % of all surgeries for the gall bladder.[2] Gall bladder carcinoma is highly lethal, as anatomic factors promote early local spread. Clinical

presentation with distant metastasis is extremely rare.[3]

The early clinical detection of gall bladder carcinoma is difficult because of its non-specific symptoms. This, along with the rapidly progressive course of the tumor resulted in poor prognosis even after surgery.[4] In the era of laparoscopy many gall bladder carcinomas are diagnosed after laparoscopic cholecystectomy & most of these tumors are in the early stage.[5] There is a direct link between gall stones and gall bladder carcinoma and incidence of cholelithiasis ranges from 54 % to 97%.[6]

Gall bladder carcinoma is more common in patients with Mirrizi,s syndrome, typhoid carriers, porcelain gall bladder, large polyps.[7] Adenocarcinoma is the most common histological type (80%) but undifferentiated carcinoma occurs in 6 % & squamous carcinoma in 3%. A variety of other lesions including adenosquamous carcinoma, carcinoid tumors, sarcoma, melanoma and lymphoma have also been found (8,9). Gall bladder carcinoma remains asymptomatic for a long time or presents with non-specific symptoms commonly related to gall stones.[10]

An ultrasound scan may show irregular thickening of gall bladder lumen and a mass in gall bladder fossa.[11] Computed tomography is better than ultrasound with positive predictive value of more than 90%.[12] Only 8.6% of the diagnoses are correct preoperatively. Incidental diagnosis "occult" with gall stone is approximately 4%.[13] A difficult gall bladder at surgery should raise the suspicious of carcinoma. The outcome & prognosis depend on time of diagnosis and the stage of the disease.

Laparoscopic or open cholecystectomy is curative if cancer is in–situ stage on histological examination of the specimen. Extended cholecystectomy involves excision of the gall bladder with regional lymphadenectomy combined with excision of the liver substance adjacent to the gall bladder. The recommended extent of liver resection varies from a non-anatomical wedge resection of the gall bladder bed to formal removal of segment IV & V including the gall bladder fossa & even right hepatic lobectomy.[14] The results of any kind of surgery are generally poor with survival rates of only a few months which depends more on stage of the disease than type of treatment provided. The overall five-year survival for gall bladder carcinoma patient is 4.1 % and one- year survival 11.8%.[15]

Aim: To evaluate patients with gall bladder carcinoma to define the demographics, modes of presentation, pathological characters and survival of such patients.

PATIENTS AND METHODS

The records of 80 patients with histologically proved carcinoma of the gallbladder seen at Gastroenterology Surgical Center, Mansoura University between 1990 to 2012 were reviewed. Patient age and sex, presenting symptoms and signs, and the technique for establishing the diagnosis were noted. The stage of disease at the time of diagnosis was compared to the duration of symptoms. Surgical procedures and other therapies were reviewed with regard to their effect on survival. Incidence of gall bladder carcinoma in comparison to other gastrointestinal malignancies, incidence of HCV infection in addition to the liver condition and associated gall stones were assessed. Patients were classified into four groups according to modes of presentation: Group I: (40 patients, 50%) presenting with gall bladder mass or obstructed gall bladder; Group II: (23 patients, 28.75%) presenting with symptomatic cholelithiases; Group III: (15 patients, 18.75%) presenting with obstructive jaundice; Group IV: (2 patients, 2.5%) presenting with GIT bleeding (one patient with hematemesis & the second patient with bleeding per rectum).

The stage of disease used was based on a classification - by Moran and Nevin: Stage I: disease localized to the mucosa; stage II: tumors that penetrate the muscularis; stage III - tumors that involve all three layers; stage IV: metastases in the cystic duct lymph nodes; and stage V: invasion or metastases to liver or to adjacent or distant organs. Treatment modalities were according to presentation, state of the tumour (local & distant) and associated liver condition (normal or cirrhotic). Routine histopathological examination of extirpated gall bladder and other excised tissues was done. No adjunctive therapy (chemo – or radiotherapy) was given to the patients. All patients were followed up by ultrasound or CT (if needed) between 3 & 6 months after surgery. Recurrence of the disease has been considered any recurrence of the tumour, distant metastases, local peritoneal seedling and port site or scar recurrence. Survival was monitored postoperatively with respect to the histological type of the tumour and the stage of the disease.

Statistical analyses: The cumulative survival rate was calculated according to the Kaplan – Meier method and correlation between survival rate & type of treatment and pathological stage was examined. P values of < 0.05 were considered statistically significant.

RESULTS

A total of eighty patients with gall bladder carcinoma were reviewed in the period 1990–2012, at the Gastroenterology Surgical Center, Mansoura University.

There were 45 males & 35 females with a mean age of 53 years (range 40-70). Gall bladder carcinoma represented 1.3% of a total of 5890 cases of abdominal malignancies with colorectal carcinoma on the top followed by hepatobiliary tumours then tumours of the stomach, esophagus and abdominal lymphoma (Table 1). In patients with gall bladder carcinoma, there was associated HCV infection in 15% of patients and gall stones in 45% but the liver was normal in 80% and cirrhotic in 20% of patients, (Table 2). Modes of presentation differed and patients were classified into 4

groups: Group I: 40 (50%) presented with obstructed gall bladder or gall bladder mass, Group II: 23 (28.75%) patients presented with symptomatic gall stones, Group III: 15 (18.75%) patients presented with obstructive Jaundice due to infiltration of the biliary system and lymphadenopathy, Group IV: 2 (2.5%) patients presented with GIT bleeding [one patient with hematemesis due to infiltration of the dudenum & the second patient with bleeding per rectum due to infiltration of the right colon, (Table 2). In -none of The 80 patients had the diagnosis been made before operation. In 72 patients (90%), diagnosis was made by the surgeon& were stage IV-V disease whereas in 8 (10%), the diagnosis was not made until the pathologist examined the specimen after laparoscopic cholecystectomy& were stage I-II disease.

Table 1. Gastro-intestinal Malignancies (5980 Cases) In the period between 1990-2012.

Item	NO	%
1. Colon & rectum	1684	28 %
2. Pancreas	1328	22.2 %
3. HCC	1300	21.7 %
4. Stomach	772	13.2%
5. Cholangiocarcinoma	456	7.7%
6. Esophagus	275	4.5%
7. Abdominal Lymphoma	85	1.4%
8. Gall bladder	80	1.3%

Treatment options varied according to heterogeneity of presentation, tumor status and condition of the liver (cirrhotic or not)(figure1). In 32 (40%) patients, extended cholecystectomy was done (en block removal of the gall bladder + wedge resection of the liver & dissection of lymph nodes in the hepatoduodenal ligament and along the hepatic artery) (Fig. 3). The sites of tumor spread were evaluated in the 26 (32,5%) patients with advanced disease, nothing done and patients treated conservatively. Invasion or metastases to the liver substance was found in 12 patients. Cystic duct, common bile duct, and peripancreatic lymph nodes were the seat of metastases in 7 patients. Diffuse carcinomatosis was seen in 4 patients. Other sites of tumor spread included the surface of the colon (two patients), the omentum, abdominal wall (one patient). In 12 (15%), right

Table 2. Patient characters.

Item	No	%
Mean age	53	
SEX		
♂	45	56
♀	35	44
HCV		
▪ +VE	12	15
▪ - VE	68	85
Liver		
▪ Cirrhosis	16	20
▪ Normal	64	80
Gall stones		
▪ Present	36	45
▪ Absent	44	55
Modes of presentations		
▪ Obstructed GB or mass	40	50
▪ Symptomatic gall stones	23	28.75
▪ Obst. Jaundice	15	18.75
▪ GIT bleeding	2	2.5

hepatectomy was done due to infiltration of the right liver lobe and right hepatic duct. Laparoscopic cholecystectomy was done for 8 (10%) patients as tumour was discovered incidentally by postoperative histopathology. The tumour in such patients did not penetrate the muscle layer, so nothing done more than simple cholecystectomy & no need for further exploration. In one patient right colon was infiltrated by gall bladder carcinoma so, extended cholecystectomy was combined with right hemicolectomy. The last patient showed infiltration of the dudenum so pancreatico-dudenectomy was done with extended cholecystectomy (Figs. 1,2). Postoperative pathology was adenocarcinoma in all patients with different grades of differentiation. As regard complications, 10 patients developed bile leak postoperatively but treated conservatively. Another one patient developed internal haemorrhage after extended cholecystectomy with pancreatico- dudenectomy and explored again to control bleeding from retropancreatic tissues. Finally one patient died in the hospital due to pulmonary embolism. Recurrences occured after a mean of 10 months in patients undergone extended cholecystectomy and it was 30 months for patients undergone simple cholecystectomy. No scar or port – site recurrences occurred in our patients. The length of survival was calculated from the date of diagnosis in the eighty patients. Comparing survival to the stage of disease at diagnosis demonstrates the expected

correlation, at least during the first year. Stage of disease was the only factor identified that consistently influenced survival. As regard survival, it was a mean of 8 months in patients with advanced gall bladder carcinoma & 21 months for those undergone extended cholecystectomy but for patients with incidental gall bladder carcinoma after laparoscopic cholecystectomies, the mean survival was 43 months. Finally the 5 year survival for patients with gall bladder carcinoma in our center was zero percent.

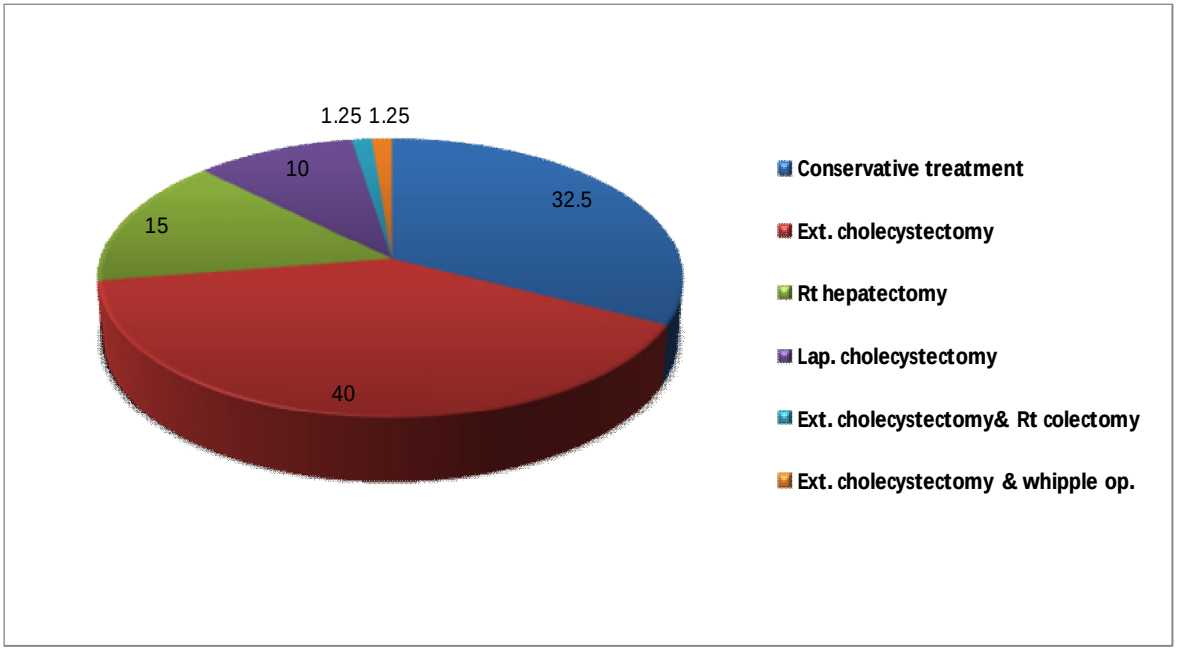


Fig 1. Treatment options.

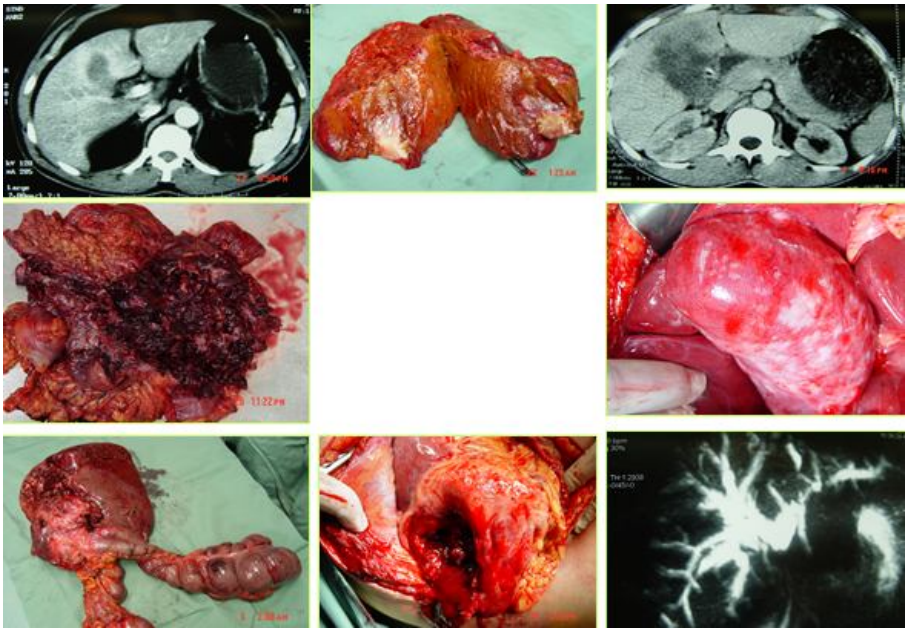
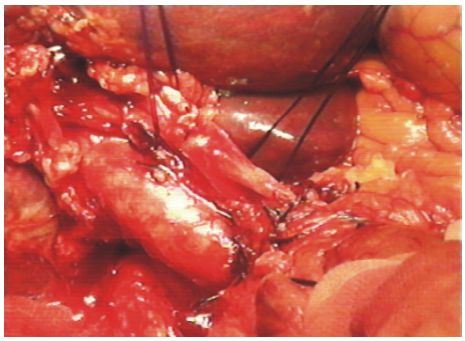
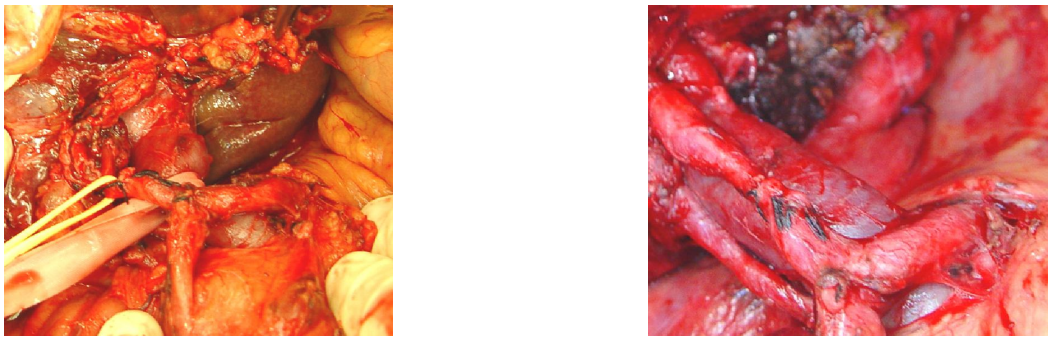


Fig. 2 Panorama of GB carcinomas.



Portahepatis lymphadenectomy



Skeletonization of portal vein & hepatic artery

Fig 3

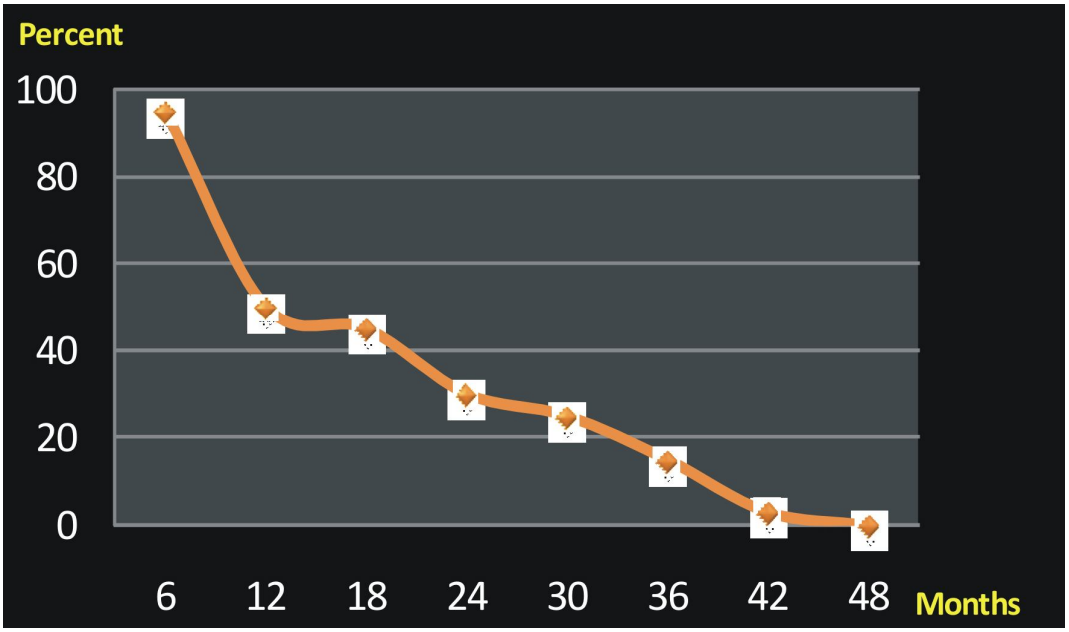


Fig 4. Estimated survival from onset of diagnosis.

DISCUSSION

A retrospective review was performed on 80 patients diagnosed with gall bladder carcinoma at Gastroenterology Surgical Center, Mansoura University between 1990 to 2012. The main objective is to characterize our institutional experience with regard to patient characters, modes of presentation, pathological characters and survival of such patients. Carcinoma of the gall bladder is the most common malignancy of the biliary tract and fifth most common cancer of the gastrointestinal tract and its incidence increases with age.[1] In our study gall bladder carcinoma represented the 8th most common cancer after colorectal, pancreatic, hepatic, gastric tumours, cholangiocarcinomma, esophageal tumours and abdominal lymphoma. Advances made in the management of other gastro – intestinal tumours have not extended to gall bladder cancer. Early diagnosis and late palliation are difficult. Clinical diagnosis of gall bladder cancer is a difficult task. In some patients the only complaints that suggest malignant disease are weight loss and anorexia. Others may present with a complication such as gastrointestinal haemorrhage. Our patients presented with obstructed gall bladder, gall bladder mass, symptomatic cholelithiasis, obstructive Jaundice & gastrointestinal haemorrhage. Cholelthiasis was present in 45% of our patients in the present series which is lower when compared to other series where gall stones were closely associated with gall bladder carcinoma.[16] The examination of choice in patients with biliary tract symptoms is ultrasonography, however, this fails to identify gall bladder cancer in early stages and it is difficult to differentiate between gall bladder cancer and cholecystitis because thickening of gall bladder wall is a feature of both diseases.[17] Selective approach to histopathological examination of gall bladder carcinoma is unsafe and unjustifiable as suspicion of malignancy is not evident despite gross examination.[18] Gall bladder cancer was not diagnosed preoperatively in any of our cases and indications for surgery were symptomatic cholelithiasis, obstructed gall bladder, gall bladder mass, obstructive Jaundice and gastrointestinal bleeding. Only in cases of advanced disease can ultrasonography show a loss of the interface between gall bladder and the liver (sign of tumour invasion), lymph nodes, dilated bile ducts and ascites, but it fails to stage the disease. CT & MRI can accurately detect gall bladder abnormalities and assess extent of the disease.[19] Today, more than 90% of cholecystectomies are performed laparoscopically and consequently the number of incidental gall bladder cancer discovered after laparoscopic cholecystectomy has increased. In our center we did 6400 cases laparoscopically and discovered 8 patients had gall bladder carcinoma by postoperative histopathology (done routinely for all cases). Fortunately the tumours did not penetrate the muscle layer in such cases so, laparoscopic cholecystectomy was sufficient and there was no need for reexploration.

The incidence of port-site recurrence is reported to be as high as 17% and the use of a retrieval bag seems not to be useful in preventing this complication. The role of prophylactic excision or irradiation of port-sites is uncertain.[20] In our series no port-site recurrences occurred. We did not use endobag routinely (except in some cases) Just to prevent rupture of the gall bladder and bile spillage during extraction and consequently wound infection. Wide cholecystectomy is the method of therapeutic choice in treating the tumour that penetrates the lamina propria into the musculature since metastases develop in the lymph nodes in 60 – 80 % of cases.[21]

However some studies[22] demonstrated that even after a seemingly radical local excision, residues occur comparatively soon.The liver resection has not led to better results.[21] The three-year survival after wide cholecystectomy is 91% compared to 28% after simple cholecystectomy[22] but in our study survival was 8 months for patients with advanced gall bladder cancer and 21 months for those undergone extended cholecystectomy and 43 months after simple cholecystectomy for incidental gall bladder carcinoma. (Fig. 4).

Five-year survival in our study is zero percent. In other series the 5-year survival is <5%.[23]

In conclusion gall bladder carcinoma is not uncommon and in-spite of modern diagnostic procedures, early diagnosis is rare & the prognosis up till now is not good. Prevention is an important goal by treating symptomatic cholelithiasis, gall bladder polyps more than 1cm and careful examination of the resected gall bladder in the operating room with frozen section for any suspicious lesion. The surgeon alone should open each extricated gall bladder and examine the wall and its interior. Finally postoperative histopathology is mandatory.

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