Presentation of Gallbladder Carcinoma and its Surgical Management

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Objective: To study the mode of presentation, age and sex distribution, socio-economic status and evaluation of various surgical methods adopted for treatment of localized and advanced gallbladder carcinoma. Design: It was a prospective type of study. Place and duration of study: This study was conducted in the Department of Surgery Nishtar Hospital, Multan from January 2004 to June 2005. Patients and methods: Twenty five patients of all ages and both sex were taken from all surgical units. On the basis of history, examination and laboratory investigations they were suspected of having gallbladder cancer. All the patients were operated and were divided into three groups on the basis of operative findings and stage of disease. Results: There were 4 males and 21 female with a male to female ratio of 1:5. Presenting feature in decreasing order of frequency were: pain in right hypochondrium in 88%, nausea and vomiting in 60%, weight loss in 40%, jaundice in 28%, anorexia in 28%, mass in right hypochondrium in 24%, pruritis in 20%, fever in 12% and ascites in 4% patients. Preoperative diagnosis of carcinoma of gallbladder was possible in 12 (48%) patients with the help of ultrasound and CT scan but all were of advanced age of disease. Gall stone were the most important etiological factor in 20 (80%) patients, obesity was found in 7 (28%) and chronic typhoid infection in 2 (8%) patients. All patients were operated. Simple cholecystectomy was done in 4 patients of stage I and II. Extended cholecystectomy done in 6 patients of stage III. Laparotomy and biopsy of the mass and/or palliative surgery for drainage of bile was done in 15 cases of stage IV and V disease. Adenocarcinoma was the most common histological type found in 22 (88%) cases. Conclusion: Gallstone are the most important etiological factor in gall bladder carcinoma.

Key words: gall stones, CA gall bladder, cholecystectomy.

Gall bladder carcinoma is the most common carcinoma of biliary tract and 5th most common malignant tumour of the elementary tract. It is more common in females with male to female ratio of 1:3. Its incidence rises with increasing age. It is found in 2% of gall bladder operations and in about 85%, gall stones are present. The clinical presentation of gall bladder carcinoma differs depending on the stage of the disease. Common presentations are pain in 89%, nausea and vomiting 52%, weight loss in 42%, jaundice in 30% and right upper quadrant mass in 23% of patients. Mostly the tumour is discovered incidentally per operatively or by biopsy report, or at an advanced stage as the symptoms of gall bladder carcinoma are generally non specific. Clinical findings in conjunction with investigation procedures like abdominal ultrasound and CT scan can raise a suspicion of malignancy. In only 10-25% of the patients the correct diagnosis is made before surgery. The tumour spreads via variety of routes. It tend to spread locally rather than by metastasis. Therefore, the challenge for the surgeon is to identify and to diagnose the disease at an early stage so that treatment can be instituted in appropriate time.

Malignancy of gall bladder is usually associated with a dismal prognosis. Adjuvant therapy is ineffective. Treatment of the gall bladder cancer is only surgical. It is potentially curable in early stages but unfortunately diagnosis is often very difficult in these cases. Surgical treatment varies from simple cholecystectomy, extended cholecystectomy and palliative surgery. The aim of the study was to determine the various modes of presentation of gall bladder cancer and its surgical management in our setup.

Patients and method:
Twenty five patients of either sex, on the basis of their history, examination and laboratory investigations were suspected of having gall bladder cancer included in this study. Patients with gall bladder carcinoma were also collected from other three surgical units. All patients were admitted in the ward and a uniform system of history taking, clinical examination and laboratory investigation were adopted. Investigations like complete blood examination, complete urine examination, blood urea, serum creatinine, liver function tests, serum electrolyte, x-ray chest, abdominal ultrasonography and CT scan were done. The information thus gathered was entered in a proforma. The patients who were unfit or unwilling for surgery were excluded from the study.

All patients were operated. Patients were stage according to UICC staging of gall bladder cancer.

Stage I Confined to mucosa/submucosa
Stage II Involvement of muscle layer
Stage III Serosal involvement
Stage IV Spread to cystic node
Stage V Invasion of liver and adjacent organs

Patients were divided into three groups on the basis of operative findings and the stage of the disease.

Group I: This group included stage I and II disease. Four patients belonged to this group. Simple cholecystectomy was done.

Group II: Comprised of stage III disease with six patients. Extended cholecystectomy (cholecystectomy with 3 cm resection
of liver parenchyma with lymph node clearance) was done.

**Group III**: It included stage IV and V disease. Fifteen patients belonged to this group. Laparotomy and biopsy of the mass or lymph nodes was done. Palliative drainage of bile was provided in 2 patients. Postoperatively patients were referred to Department of Oncology, Nishtar Hospital Multan.

**Results:**
Among the 25 patients, there were 21 (84%) females and 4 (16%) males. Female to male ratio was 5:1. The decade wise age and sex distribution of the patients (Fig. 1).

All the 21 female patients were married. 18 (85.7%) were housewives or worked with their husband in the form. One female was a headmistress, other was a lecturer and one worked in office as receptionist. Among the male patients 2 (50%) were labourers while remaining 2 (50%) were gazetted government officers. Thus out of 25 patients only 5 (20%) belonged to middle or upper class while 20 (80%) patients belonged to poor socioeconomic class.

Twenty (80%) patients were residents of rural areas or smaller towns while 5 (20%) patients belonged to big cities. The prevalence of various clinical findings observed is shown in Figure 2. Pain in right hypochondrium, nausea and vomiting, weight loss, jaundice and mass right hypochondrium were most common findings, while fever and ascites were the least.

Several etiological factors have been associated with carcinoma of gall bladder. In present study gall stones were present in 20 (80%) of the patients, obesity was found in 7 (28%) patients and chronic typhoid infection in 2 (8%) patients. Table 1 shows findings of various laboratory investigations.

Preoperative diagnosis of carcinoma of gall bladder was possible in 12 (48%) patients with the help of ultrasound but all these patients had advanced disease. CT scan was done in only 12 patients and it was helpful in 9 patients. All patients underwent operation, carcinoma was localized to gall bladder in 4 (16%) cases. Spread to right lobe of liver in 5 cases, local lymph nodes were enlarged in 5 cases and generalized peritoneal dissemination in 1 patient. There was extensive involvement of regional lymph node, common bile duct, cystic duct and right lobe of liver in remaining 10 patients.

Table 2 shows various stages in patients of gall bladder carcinoma. Patients were divided into three groups on the basis of operative findings and the stage of disease.

<table>
<thead>
<tr>
<th>Stage of Disease</th>
<th>=n</th>
<th>%age</th>
</tr>
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<tbody>
<tr>
<td>Stage I</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Stage II</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>Stage III</td>
<td>6</td>
<td>24</td>
</tr>
<tr>
<td>Stage IV</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>Stage V</td>
<td>10</td>
<td>40</td>
</tr>
</tbody>
</table>

Table 3 shows various operative procedures done in patients of carcinoma gall bladder. In our study 22 (88%) patients had adenocarcinoma, 2 (8%) had squamous cell carcinoma and 1 patient had carcinoma in situ.

Postoperative radiotherapy was given following operative procedure in the department of oncology but results were not promising. Prognosis was good in patients with incidentally discovered gall bladder carcinoma. Out of 4 patients 3 are still alive and attending our OPD. In advanced stages of disease prognosis was very poor.

Fig. 1: Decade wise age and sex distribution of the patients

Fig. 2: Prevalence of various clinical features

<table>
<thead>
<tr>
<th>Findings of Investigations</th>
<th>=n</th>
<th>%age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased haemoglobin</td>
<td>15</td>
<td>60</td>
</tr>
<tr>
<td>Increased ESR</td>
<td>15</td>
<td>60</td>
</tr>
<tr>
<td>Increased total leucocyte count</td>
<td>9</td>
<td>36</td>
</tr>
<tr>
<td>Increased serum bilirubin</td>
<td>7</td>
<td>28</td>
</tr>
<tr>
<td>Increased serum alkaline phosphate</td>
<td>7</td>
<td>28</td>
</tr>
<tr>
<td>Increased SGOT &amp; SGPT</td>
<td>7</td>
<td>28</td>
</tr>
</tbody>
</table>

Table 1: Laboratory investigations

Table 2: Staging of carcinoma of gall bladder

Table 3: Operative procedures
Discussion:
Carcinoma of the gall bladder is the commonest malignancy of biliary tract\(^1\). It is usually asymptomatic in its early course therefore most patients present with an advanced disease\(^3\). In present study highest incidence of carcinoma of gall bladder is in fifth decade of life. These figure show involvement at relatively younger age as compared to Western society, where average age of involvement is sixth decade of life\(^6\). Carcinoma of gall bladder like other biliary tract diseases is more common in females\(^2\,\,^4\,\,^7\). In our study there were 21 females and 4 males with male to female ratio of 1:5. Gall stones and chronic inflammation are most common etiological factors present in 75-90% cases of CA gall bladder\(^8\). In our study, coexisting stones were seen in 20 (80%) cases which is almost similar to the reported incidence from Chile\(^3\) (85%). Other factors were obesity\(^8\), ileal bypass, typhoid carrier\(^9\) and industrial pollution. In our study 48% patients were obese and 8% having chronic typhoid infection.

The comparison of clinical features in present study with other studies is shown in Table 4.

In present study, carcinoma was an incidental finding in 16% patients on histopathological examination. Preoperative diagnosis was possible in 12 (48%) patients with the help of ultrasound. However all these patients were of advanced stage disease. This result is much lower than that described by Kumar S et al\(^{10}\) (89%). Computerized tomography scan has been used to detect malignancy. Kumar S and colleagues showed that 78% of carcinoma of gall bladder could be diagnosed correctly with CT scan\(^{10}\). CT scan was done only in 12 patients who could afford it and was helpful in diagnosing 75% cases.

The hepatobiliary system can be visualized by a variety of imaging techniques. USG is the best method of investigation. USG-guided FNAB is a safe and accurate technique to diagnose advanced gall bladder malignancy\(^11\). MRI and MRCP can provide information relevant to preoperative staging of gall bladder carcinoma\(^12\).

Patients with gall bladder carcinoma usually present very late. In present study disease was localized to gall bladder in 4 patients (16%) while in remaining 21 (84%) patients, disease had advanced to stage III, IV and V. Thus out of 25 patients only 4 patients were of early stage carcinoma. Extended cholecystectomy was done in 6 patients of stage III disease while in remaining 15 patients exploratory laparotomy and biopsy was done. Palliative drainage for bile was provided in 2 patients, in one internal drainage by bilioenteric bypass and in other external drainage.

Adenocarcinoma is the commonest type\(^3\,\,^11\) of gall bladder carcinoma followed by squamous cell carcinoma. In our study, 22 (88%) patients had adenocarcinoma and 8% had squamous cell Ca and 4% carcinoma in situ.

Table 4: Comparison of clinical features in patients with Ca gall bladder

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>A%</th>
<th>B%</th>
<th>C%</th>
<th>D%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain right upper quadrant</td>
<td>88</td>
<td>89</td>
<td>76</td>
<td>82.7</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>60</td>
<td>52</td>
<td>32</td>
<td>44.8</td>
</tr>
<tr>
<td>Weight loss</td>
<td>40</td>
<td>42</td>
<td>39</td>
<td>35</td>
</tr>
<tr>
<td>Jaundice</td>
<td>28</td>
<td>30</td>
<td>38</td>
<td>36</td>
</tr>
<tr>
<td>Anorexia</td>
<td>28</td>
<td>---</td>
<td>---</td>
<td>20</td>
</tr>
<tr>
<td>Abdominal mass</td>
<td>24</td>
<td>25</td>
<td>25</td>
<td>60</td>
</tr>
<tr>
<td>Pruritis</td>
<td>20</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Fever</td>
<td>12</td>
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</tbody>
</table>

A% = Percentage of symptoms in our study
B% = Percentage of symptoms described by Malik et al (2003)
C% = Percentage of symptoms described in Cuschiati\(^7\).
D% = Percentage of symptoms described by Cunningham et al (2002)\(^13\)

Conclusion:
This study concludes that gall stones are the most important etiological factor of gall bladder carcinoma. Therefore a suspicion of malignancy should always be kept in mind in long standing cases of cholelithiasis. Early cholecystectomy is advisable in patients who are suffering from gall stones because long term survival can be expected in incidentally discovered gall bladder carcinoma.

References: