Incidental Carcinoma Gallbladder Cases in Routine Cholecystectomy

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ABSTRACT
Background:
Gallstone is a very common gastrointestinal disorder. It is known to produce histopathological changes in the gallbladder. It is also one of the predisposing factors for the development of cancer of gallbladder. Most of the carcinoma of gallbladder is diagnosed as incidental finding among patients undergoing cholecystectomy. This study was carried out to find out cases of incidental carcinoma gallbladder in patients operated for cholecystitis.

Methods:
This is a hospital based descriptive study conducted in Department of Pathology at Nepalgunj Medical College Teaching Hospital, Kohalpur from April 2015 to March 2016. Total of 260 surgical specimens of gallbladder were included in the study.

Results:
In this study, there were 5 cases of incidental carcinoma gallbladder (1.92%). In the carcinoma patients, the mean age was 56 years with M: F ratio 1:4. Adenocarcinoma of the gallbladder was the most common malignancy of the gallbladder.

Conclusion:
Histopathology is a gold standard method for detection of carcinoma of gallbladder, as it is superior to clinical and radiological examination.

Routine histopathological study of all cholecystectomy specimens are suggested as it helps in diagnosing occult gallbladder carcinomas.

Key words: Carcinoma Gallbladder, Cholecystectomy, Cholecystitis, Histopathology, Incidental.

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INTRODUCTION
The gallbladder is a pear shaped sac attached to the posteroinferior aspect of the right hepatic lobe. In the adult, it measures up to 10 cm in length and 3 to 4 cm in width. The gallbladder is divided into the following regions: fundus, body, and neck. The portion of the body that joins the neck is referred to as the infundibulum; sometimes there is a small bulge in this portion, known as Hartmann pouch.

The gallbladder via the cystic duct joins with the common hepatic duct to form the common bile duct that empties into the duodenum. The primary function of the gallbladder is to concentrate and store hepatic bile and deliver bile into the duodenum in response to a meal.

Gallbladder cancer is a disease of the elderly; it affects patients in their 70s, with a female to male
RESULTS

A total of 271 cholecystectomy specimens were received in our department. Eleven cholecystectomy specimens were excluded either due to autolytic changes or inadequate clinical details. Most of the cases diagnosed histopathologically were acute or chronic calculus cholecystitis (94.6%), 7 patients had dysplasia (2.7%), 1 patient each had adenoma and hydrops gallbladder (0.4%). There were 5 cases of incidental finding of carcinoma gallbladder (1.92%). Six patients were operated for gallbladder polyp but on gross examinations no polyps were identified in any of the six specimens. Among chronic cholecystitis, its variants included follicular cholecystitis, xanthogranulomatous cholecystitis and follicular cholecystitis in 5 cases each.

None of the cases were suspected pre or intraoperatively to have gallbladder carcinoma. Out of the 5 cases of GB carcinoma, 4 were adenocarcinoma and 1 was undifferentiated carcinoma. All 5 patients had associated stones and were non vegetarians.

The age ranged from 16 to 77 years with a mean age of 39.58 years. Most patients were in the age group 31 to 40 years (30%) followed by 21 to 30 years (25.8%) and 41 to 50 years (20.8%). Male patients were 37 and 223 were females. There was a female preponderance in this study with M: F ratio 1:6.

A clinical diagnosis of chronic cholecystitis was made in 93.8% of the cases which increased to 95% after USG. Most of the cholecystectomies were performed for calculus cholecystitis (95%). The histological diagnosis were narrowed down into 5 diagnosis for statistical purposes which included adenoma (0.4%), carcinoma (1.9%), chronic cholecystitis (94.6%), dysplasia of gallbladder (2.7%) and hydrops gallbladder (0.4%).

Gallbladder cancer was detected in 5 (1.92%) cases and was more common in females (M: F ratio 1:4). The mean age of occurrence was 56 years. Majority of the patients who were diagnosed as carcinoma presented with abdominal pain, dyspepsia, weight loss, anorexia, nausea, malaise, pruritus and vomiting. Generally patients with carcinoma have delayed onset of symptoms.
Table 1: Clinicopathological Features of Carcinoma Gallbladder

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>Sex</th>
<th>USG findings</th>
<th>Gross findings</th>
<th>Type of tumor</th>
<th>Stage (TNM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>66</td>
<td>F</td>
<td>Calculus cholecystitis</td>
<td>No significant findings</td>
<td>Well differentiated adenocarcinoma</td>
<td>T2NxMx</td>
</tr>
<tr>
<td>55</td>
<td>F</td>
<td>Calculus cholecystitis</td>
<td>No significant findings</td>
<td>Poorly differentiated adenocarcinoma</td>
<td>T1BnMx</td>
</tr>
<tr>
<td>49</td>
<td>F</td>
<td>Calculus cholecystitis</td>
<td>No significant findings</td>
<td>Well differentiated adenocarcinoma</td>
<td>T2NxMx</td>
</tr>
<tr>
<td>42</td>
<td>F</td>
<td>Calculus cholecystitis</td>
<td>Polypoidal projection in the mucosa</td>
<td>Well differentiated adenocarcinoma</td>
<td>T2NxMx</td>
</tr>
<tr>
<td>77</td>
<td>M</td>
<td>Calculus cholecystitis</td>
<td>Adenoma</td>
<td>Undifferentiated carcinoma</td>
<td>T3NxMx</td>
</tr>
</tbody>
</table>

DISCUSSION
Among patients who were diagnosed as carcinoma gallbladder, the mean age was 56 years with M: F ratio 1:4. This finding is similar to the retrospective analysis of 52 patients in which the mean age of gallbladder cancer was 51.5 years and more than 80 percent of cases were females.  

Similar finding had been reported in several studies from Indian subcontinent which showed gallbladder cancer affects predominantly female in their fourth and fifth decade of life. However, studies from other part of the world has shown that gallbladder cancer was predominant in females with peak incidence in sixth and seventh decade of life. The reason for gallbladder cancer developing at a younger age in Indian subcontinent population including Nepal, could be because, gallstones develop at a younger age in Indian subcontinent population than western population, and gallstone is important risk factor for development of cancer. This age difference of gallbladder cancer patients from western population might be over-estimated, as the life expectancy in Nepal is low (male 68 and female 71 years).

Gallstones appear to be the most important risk factor, being reported in 98% cases of gallbladder cancer. Though gallstones are very often implicated with gallbladder carcinoma, other factors tend to increase the risk include porcelain gallbladder, chronic infection with Salmonella typhi, carcinogen exposure (eg. miners exposed to radon), and abnormal pancreatobiliary junction. Most of the cases of carcinoma GB are diagnosed at advanced stage and have a poor prognosis having 5 year survival rate of <5%. When detected at early stages prognosis may improve significantly up to 90-100% five years survival rate.

The incidence of incidental GB carcinoma in routine post-cholecystectomy cases was 1.92%, Amanullah et al (1.8%), Shrestha R et al (1.4%) 22 and Ghimire P et al (1.28%) 23 have found the incidence similar to ours whereas Zhang WJ et al has shown it occurrence as low as 0.19% and Naqvi et al has found its occurrence as high as 5.9%. Autopsy studies indicate that only 1-4% of patient with cholelithiasis develop cancer compared to <0.2% of those not containing stones. Most of the studies listed in table no.2 show similar findings.

Table 2: List of Various Studies Showing Incidence of Incidental Carcinoma Gallbladder. 27-29

<table>
<thead>
<tr>
<th>Studies</th>
<th>Year</th>
<th>Place</th>
<th>Sample size</th>
<th>M:F</th>
<th>Mean age (year)</th>
<th>Incidence of CG GB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duphna et al</td>
<td>2006-2015</td>
<td>Nepal</td>
<td>1697</td>
<td>1:5</td>
<td>70</td>
<td>0.3%</td>
</tr>
<tr>
<td>Khoos JJ &amp; Narul AM</td>
<td>1998-2007</td>
<td>India</td>
<td>1206</td>
<td>1:5</td>
<td>56.2</td>
<td>0.99%</td>
</tr>
<tr>
<td>Mittal R et al</td>
<td>2006-2015</td>
<td>Malaysia</td>
<td>1122</td>
<td>1:2</td>
<td>56.7</td>
<td>0.62%</td>
</tr>
<tr>
<td>Zhang WJ et al</td>
<td>2006-2015</td>
<td>China</td>
<td>10,466</td>
<td>1:4</td>
<td>65.7</td>
<td>0.19%</td>
</tr>
<tr>
<td>Amanullah et al</td>
<td>2006-2015</td>
<td>India</td>
<td>428</td>
<td>1:7</td>
<td>47</td>
<td>1.87%</td>
</tr>
<tr>
<td>Shrestha R et al</td>
<td>2006-2015</td>
<td>Nepal</td>
<td>570</td>
<td>1:3</td>
<td>53.56</td>
<td>1.4%</td>
</tr>
<tr>
<td>Naqvi et al</td>
<td>2006-2015</td>
<td>Pakistan</td>
<td>1160</td>
<td>1:4</td>
<td>-</td>
<td>5.9%</td>
</tr>
<tr>
<td>Ghimire P et al</td>
<td>2006-2015</td>
<td>Nepal</td>
<td>783</td>
<td>1:3</td>
<td>68.3</td>
<td>1.28%</td>
</tr>
<tr>
<td>Recent study</td>
<td>2015-2016</td>
<td>Nepal</td>
<td>260</td>
<td>1:4</td>
<td>56</td>
<td>1.92%</td>
</tr>
</tbody>
</table>

CONCLUSION
The histopathological spectrum of gallbladder disease after cholecystectomy was found to be quite diverse. The most common histopathological diagnosis in gallstone disease was chronic cholecystitis, which was associated with a variety of mucosal alterations and lesions like cholesterosis, metaplasia, dysplasia and adenomyoma. Increased rate of carcinomas was also seen in our study, which reinforces the importance of histopathological examination in all routine cholecystectomy specimens.

It is a standard practice to perform routine histopathological examinations for all cholecystectomy specimens. Various studies including the working reporting of Royal College of Pathologists have recommended for this routine standard practice.

REFERENCES
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