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Does Routine Histopathological Examination of Gallbladder after Simple Cholecystectomy Add Additional Value?

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Background: Cholecystectomy for gallbladder stone disease is a common surgical procedure. Gallbladder carcinoma is a rare malignancy with poor prognosis, which has been linked in some studies to pre-existing gall stone disease. The current practice is to send all gallbladder specimens after cholecystectomy for histopathological examination. This adds additional workload on the pathologists.

Objective: To determine the necessity of routine histopathological examination of gallbladder specimens following simple cholecystectomy.

Setting: Aseer Central Hospital, Abha, Saudi Arabia.

Design: Retrospective cohort study.

Method: Patients who had cholecystectomy for gallstone disease from April 2010 to March 2012 were included. Operative notes, histopathological reports and final diagnoses were reviewed.

Result: The study included 803 patients who had simple cholecystectomy. Three of these patients were found to have gallbladder carcinoma, two females and one male. Dense adhesions were encountered in all malignant cases necessitating conversion from laparoscopic to open cholecystectomy in one case. Macroscopic examination revealed a thickened gallbladder in all three patients; two patients had mucosal papillary lesions and one patient had polypoidal projection and mucosal ulcerations. These findings were confirmed by the pathologist. On microscopic examination, two patients had adenocarcinoma while one patient had neuroendocrine tumor.

Conclusion: Selective approach for sending gallbladder specimens after cholecystectomy seems justifiable with no compromise on detection of incidental gallbladder cancer. This approach would lead to a reduction of workload on the pathologist.

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Adenocarcinoma of the gallbladder is a rare malignancy accounting for about 0.5-1% of all gastrointestinal malignancies[1]. It is a very aggressive neoplasm with extremely poor prognosis; 5-year survival rate is 5-15%[2]. Chronic inflammation in the gallbladder wall due to gallstones is considered a risk factor for carcinoma. It is estimated that 85% of cases are associated with gallstones[3]. In spite of the great advances in the field of radiological investigations, gallbladder carcinoma is very rarely diagnosed preoperatively. Suspicion is usually intra-operative and the diagnosis is usually confirmed after histopathology[1].

The current practice is to send all specimens for routine histopathology which increases the workload on the pathologists[4-5]. Therefore, the question remains as to whether there is a need to send all gallbladder specimens for histopathological examination after surgery since it does not necessarily alter the management or provide an absolute advantage.

Cancer of the gallbladder is known to vary greatly in incidence[6]. There is no statistics in the literature about the incidence of gallbladder stones or incidence of gallbladder cancer in the southern region of Saudi Arabia.

The aim of this study is to assess the necessity of routine histopathological examination of the gallbladder following simple cholecystectomy.

METHOD

A retrospective review of all patients who had cholecystectomy for gallstone disease from April 2010 to March 2012 was conducted. The histopathological reports of these patients were reviewed.

Data of preoperative laboratory investigations, imaging (Ultrasound or CT scans), intraoperative findings, macroscopic appearance of the specimen and histopathology reports of patients with incidental gallbladder malignancy were carefully analyzed. The AJCC TNM system was used as reference for staging carcinoma gallbladder[7].

RESULT

The study included 803 patients who had simple laparoscopic cholecystectomy. The mean age of the patients was 41.3±14.7 years. Female to male ratio was 3:1. According to histopathological reports, the findings were classified into inflammatory or neoplastic, see table 1.

Table 1: Histopathology Results of All Patients (N=803)

Pathological Type	Number (Percentage)
Inflammatory	
Chronic Calculous Cholecystitis	659 (82.1)
Acute Calculous Cholecystitis	121 (15.1)
Neoplastic (Benign Lesions)	
Cholesterolosis	16 (2)

Xanthogranuloma	4 (0.5)
Malignant Lesions	3 (0.4)

Three cases were found to have gallbladder carcinoma, two females and one male, with a mean age of 68.7±4.2 years. The hospital based prevalence of incidental cancer of gallbladder after cholecystectomy was 3 (0.4%). Dense adhesions were encountered in all malignant cases. In two patients, the procedure was completed by laparoscopy, while in the third patient; it was converted to open cholecystectomy due to the presence of dense adhesions and inability to define the anatomy of Calot's triangle. Preoperative and operative data are shown in table 2.

Table 2: Preoperative and Intraoperative Data for Patients with Incidental Gallbladder Cancer

Preoperative & Operative Data	Patient One	Patient Two	Patient Three
Preoperative Diagnosis	Chronic Calculous Cholecystitis	Obstructive Jaundice	Acute Cholecystitis
Preoperative Imaging	Chronic Calculous Cholecystitis	Chronic Calculous Cholecystitis with Peri-Cholecystic Fat Stranding	Acute Cholecystitis with Mild Pericholecystic Fluid Collection
Preoperative Suspicion	No	No	No
Procedure	Laparoscopic Cholecystectomy	ERCP Followed by Laparoscopic Cholecystectomy	Laparoscopic Cholecystectomy Converted to Open Cholecystectomy
Operative Findings	Severe Adhesions, GB Filled With Pus, Thickened Wall GB	Severe Adhesion, Difficulty in Identifying Anatomy	Severe Adhesions, GB Filled with Pus, Thickened Wall GB, Difficulty in Identifying Anatomy

Histopathological report showed macroscopic abnormalities to be found in all three patients with gallbladder carcinoma. All patients had a thickened gallbladder, 2 (66.7%) had mucosal papillary lesions, one (33.3%) patient had polypoid projection and mucosal ulcerations. Microscopically, two patients had adenocarcinoma while one patient had neuroendocrine tumor, see table 3. Further management and survival are shown in table 4.

Table 3: Pathological Study of Specimens with Incidental Gallbladder Cancer

Pathology	Patient One	Patient Two	Patient Three
Macroscopic Appearance	Papillary Structures Measuring 3x2.5 cm	Multiple Foci of Small Papillary Structures on Mucosal Layer	Focal Polypoidal Thickening in the Fundus Region Measuring 3x2 cm with Mucosal Ulceration
Histopathology	Well Differentiated Adenocarcinoma	Moderately Differentiated Adenocarcinoma	Moderately Differentiated Neuro-Endocrinal Tumor
TNM	T3 N0 M0	T2 Nx M0	T3 Nx M0

Table 4: Follow-up of Patients with Incidental Gallbladder Cancer

Follow-up	Patient One	Patient Two	Patient Three
Further Management	Referred to a Higher Center Where Segmental Liver Resection Was Done	Referred to a Higher Center where No Further Surgery Was Decided (Follow-up)	Patient Refused Follow-up

Survival	Alive After 18 Months of Diagnosis	Alive After 15 Months of Diagnosis	Died after 13 Months of Diagnosis

DISCUSSION

Surgical treatment is the treatment of choice for patients with gallbladder cancer[8]. In order to achieve the R0 resection, early diagnosis of cancer is the main hope for cure of such patients. For patients with low pathological staging (up to pT2a), simple cholecystectomy is sufficient. On the other hand, radical cholecystectomy which is a major surgery including removal of the gallbladder, segment IVb and V of the liver, in addition, to regional lymphadenectomy is considered the surgical option for cancers with pathological staging (pT2b and more)[9]. Cuccinotta et al found that the most important factor determining the outcome of incidental gallbladder adenocarcinoma is related to tumor stage rather than the surgical approach[10].

The high incidence (74-92%) of mixed pathology (neoplastic and inflammatory) makes the preoperative diagnosis very difficult[11]. In our study, all three patients with incidental gallbladder cancer were associated with cholelithiasis and had variable presentations; chronic calculous cholecystitis, obstructive jaundice, and acute calculous cholecystitis. A common factor in patients with incidental gallbladder cancer in our findings was old age. All patients were above 60 years. Gallbladder carcinoma may be intimately associated with large or numerous cholesterol gallstones, which might interfere with the mechanical functioning of the gallbladder. In addition, gall stones cause chronic mechanical damage to the gallbladder mucosa[6]. The findings of the present study support the hypothesis that gallbladder carcinoma is an age-related malignancy that may be intimately associated with long-standing benign gallstone disease of the gallbladder.

Another common factor in patients with incidental gallbladder cancer in this study was the dense adhesions found during surgery where one patient's operation was converted to open cholecystectomy due to inability to identify the anatomy. The gallbladder was full of pus in two cases and in one case, dense adhesions were found with no obvious explanation. Macroscopic findings were found in all cases of gallbladder cancer. Earlier studies have shown that the surgeon can expect abnormal pathology intra-operatively even if there was no suspicion preoperatively[2,6]. The existence of pus does not exclude the existence of other pathology in the specimen[11]. Histopathological examination revealed adenocarcinoma in two patients, and they were referred to a specialized center for therapy. One of them was re-operated (radical surgery) while the other is under follow up. Both are alive 18 and 15 months after diagnosis of gallbladder cancer. The third patient was reported to have small cell neuroendocrine carcinoma, which is a very rare type of gallbladder cancer. This patient refused any type of further management or follow-up and died 13 months after the diagnosis.

Although the current practice is to do routine histopathological examination for all cholecystectomy specimens, we think this has to be re-evaluated. In our study of 803 specimens, incidental gallbladder cancer was found in three (0.37%). All these had dense adhesions intra-operatively. In addition all of them had macroscopic findings as papillary and polypoidal masses or mucosal ulceration. There were no cases of carcinoma gallbladder in specimens which were normal on macroscopic examination.

The gallbladder specimens constitute 23% of the general surgery load for the pathologist in our hospital; it would save cost to follow a selective approach for sending the specimen of gallbladder. In addition it will decrease the workload on the pathologists. Selective approach should strictly include any suspicion: preoperative imaging, intraoperative or postoperative as the surgeon opens the gallbladder specimen and examines it carefully by inspection and palpation. If there is any macroscopic abnormality, the specimen should be sent for histopathological examination.

Early stage gallbladder carcinoma may be difficult to distinguish from chronic cholecystitis, as they both present as thickened gallbladder[8]. This possibility is very rare and was not present among our 803 patients. Tumors that are not seen or felt macroscopically are described to be of low stage and cholecystectomy alone is considered curative for them. Similar findings to our study were found in recent studies; Dix et al found gallbladder malignancy in 5 out of 1,308 patients (0.38%)[11]. All of these cases had a demonstrable macroscopic abnormality on gross examination; Bazoua et al found 5 cases of gallbladder malignancy in 2,890 consecutive cases (0.17%)[12]. Again all of these patients had visible macroscopic abnormal findings. Mattil et al found 13 cases of gallbladder cancer among 1,305 patients (1%) with macroscopic abnormalities in all 13 cases[13].

The limitations of this study are being a retrospective, non-randomized, single center study and short period of follow-up.

CONCLUSION

Selective approach for sending the specimens of gallbladder after simple cholecystectomy seems justifiable; it will decrease the workload on pathologists with no compromise on detection of incidental gallbladder cancer. However, further prospective multi-center study is required to support our findings.

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