Original Article

Gall Bladder Carcinoma in Patients Undergoing Cholecystectomy for Cholelithiasis

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Abstract

Objective: To determine the proportion and timing for suspecting the diagnosis of gall bladder carcinoma in patients undergoing cholecystectomy for cholelithiasis.

Methods: A retrospective study conducted at the Aga Khan University Hospital, Karachi over a period of six years, included medical records of patients, with cholecystectomy for cholelithiasis and a histopathological diagnosis of gall bladder carcinoma. An extensive review was done with special reference to the features of suspected or unsuspected gall bladder carcinoma. Timing of suspicion was categorized on the basis of clinical features, investigations, operative and histopathological findings.

Results: Out of 1396 cholecystectomies performed during the period of study, sixteen patients (1.15%) were diagnosed as gall bladder carcinoma. Only three patients had pre-operative ultrasonographic features to raise suspicion for gall bladder malignancy whereas eight patients were suspected to have a malignant lesion, on the operative findings. Five patients were missed and the diagnosis was established after histopathological examination.

Conclusion: The ultrasonography can miss a significant number of malignant lesions of the gall bladder and every cholecystectomy specimen should be examined histologically (JPMA 55:497;2005).

Introduction

Carcinoma of gall bladder is the most common malignancy of biliary tract and is the 7th most common carcinoma of the gastrointestinal tract.[1] In our population, gall bladder carcinoma contributes to 3.6% to 4.8% of female malignancies.[2,3] One of the local studies has reported this to be the commonest malignancy of gastrointestinal tract in females.[3] Although the youngest reported case of gall bladder carcinoma occurred in an 11 years old Navajo girl[4], the peak incidence of gall bladder carcinoma is observed in the 6th and 7th decades of life. Cholelithiasis has consistently been shown to be associated with carcinoma of the gall bladder but the definitive causal relationship has not yet been established.

The rationale for conducting this study was the hypothesis that the diagnosis of gall bladder carcinoma is missed in some of those patients whose gall bladder specimens are not sent for histopathological examination due to financial constraints.

The objective of this study was to determine the proportion and timing of suspecting the diagnosis of gall bladder carcinoma in patients undergoing cholecystectomy for cholelithiasis at a tertiary care centre of an underdeveloped country.

Patients and Methods

A retrospective analysis of the medical records of patients, subjected to cholecystectomy for cholelithiasis and had the histopathological diagnosis of gall bladder carcinoma was performed. Patients admitted in the Aga Khan University Hospital, Karachi over a period of six years from 1993 to 1998 numbered 119679. Of these, 102 patients were diagnosed as carcinoma gall bladder, based on histopathological examination, which amounts to 1.17 gall bladder carcinoma per 1000 patients admitted per year. During the same period, 1396 cholecystectomies were performed for cholelithiasis. Of these, 443 patients had open cholecystectomy whereas 953 patients underwent laparoscopic cholecystectomy. The indications for open cholecystectomy were acute cholecystitis, Empyema of gall bladder, patient being unfit for laparoscopic procedure due to associated co-morbidities and fewer consultants having expertise in laparoscopic procedures during the initial period of the study.

The inclusion criteria were, pre-operative ultrasonographic diagnosis of cholelithiasis, patients undergoing cholecystectomy, histopathological diagnosis of gall bladder carcinoma, and any pre-operative feature raising the suspicion of gall bladder carcinoma on retrospective evaluation of the medical record but no such suspicion stated in the medical record itself.

The exclusion criteria included pre-operative diagnosis of gall bladder carcinoma, any pre-operative suspicion of gall bladder carcinoma mentioned in medical records, absence of cholelithiasis and histopathological diagnosis other than gall bladder carcinoma.

Pre-operative suspicion for carcinoma gall bladder

was considered, when the clinical features and ultrasonography results had mentioned it as such in the records. When the operative findings were suggestive of gall bladder malignancy, it was intra-operative suspicion.

When the histopathology examination gave a diagnosis of carcinoma gall bladder, it was called post-operative suspicion.

Results

This retrospective search of medical records revealed 16 patients fulfilling the selection criteria and their main features mentioned in table 1 with special reference to the suspicion of gall bladder carcinoma. The mean age of the patients studied was 58.4 years with the range being 35 to 84 years. Of these 16 patients, 14 were females and 2 males. All patients included in the study had gallstones on ultrasonography and underwent cholecystectomy for cholelithiasis. About half of these patients had thick walled gall bladder whereas irregular thickening of wall was observed in only three patients. Ten patients underwent open cholecystectomy whereas only one patient successfully completed laparoscopic cholecystectomy. Five procedures were started as laparoscopic cholecystectomy but had to be converted to open technique due to operative findings/problems. The retrospective evaluation of medical records raised some degree of pre-operative suspicion of gall bladder carcinoma on the basis of clinical features and ultrasonographic features in only about one-fifth of the patients but no such suspicion was mentioned in the medical records itself. About half of the patients had a palpable gall bladder during surgery which was suspected to be cancerous. More than 30% of the patients were not suspected to have gall bladder carcinoma prior to the histopathological examination. One of the pre-operatively suspected as well as four of the intra-operatively suspected cases were initiated as a laparoscopic procedure but had to be converted to the open technique. The only successfully completed laparoscopic procedure was of the patient who was not suspected for gall bladder carcinoma even after the surgery but prior to the histopathological examination.

Table 2 shows the comparison of this study results with other published work with respect to timing of suspicion for carcinoma of gall bladder.

Table 2. Timing of suspicion for gall bladder carcinoma.

Study	Total Patients	Pre-Operative/ Intra-Operative	Post-Operative
Fung Y et al[25]	42	22	20
Yamaguchi K et al[5]	24	10	14
Current Study	16	11	5

Discussion

The western literature review revealed that 0.3% to 2.85% of the patients who underwent cholecystectomy for presumed benign disease were found to have carcinomas of gall bladder.[5-8] The proportion of gall bladder carcinoma detected in patients undergoing cholecystectomy for cholelithiasis in this study was 1.15% and is quite comparable with the western literature.[5-8] In contrast to this, some local studies have reported that 4% to 12% of the patients undergoing cholecystectomy for cholelithiasis had gall bladder carcinoma.[9-12] This significantly high ratio of gall bladder carcinoma is probably due to inadequate pre-operative evaluation.

The timing of suspicion for carcinoma of gall bladder in this study is compared with other studies in table 2. This issue of timing of suspecting carcinoma is extremely important for the management of the gall bladder carcinoma as Tis and T_1 tumors can be effectively treated with simple cholecystectomy but T_2 or more advanced lesions need radical resection.[5,13] However, some authors recommend radical resection even for early gall bladder carcinoma (confined to the mucosa or muscularis layer) in view of the possibility of lymph node metastases in the early stages.[14] Good prognosis is anticipated in patients with gall bladder carcinoma discovered as an incidental findings.[8] These cases have a relatively early stage of the disease and rarely show lymphatic or venous invasion.[13,14]

The lack of specific signs and symptoms at an early and resectable stage retards the diagnosis of gall bladder carcinoma. The clinical manifestations of gall bladder carcinoma are usually identical to those of cholecystitis and cholelithiasis and occur insidiously with the advancement of the disease. The incidence of gallstones in patients with gall bladder carcinomas ranges from 60% to 98%.[6,8,15] It is presumed that longstanding chronic inflammation by cholelithiasis plays a role in carcinogenesis.

Table 1. Analysis of suspicion of gall bladder carcinoma.

Suspected or Unsuspected	Number of patients	Mean age (years)	Ultrasonographic findings			Operative findings		
			Gallstones	Thick walled	Irregular wall	Polypoid mass	Palpable gall bladder mass	Enlarged lymph node at porta hepatis
Pre-Operatively Suspected	3	46.7	3	2	3	1	2	2
Intra-Operatively Suspected	8	58.3	8	4	0	0	7	3
Unsuspected	5	65.4	5	2	0	0	0	0

Despite marked advances in biliary tract imaging, diagnostic accuracy is not satisfactory in cases of gall bladder carcinomas. Abdominal ultrasonography is a valuable screening imaging modality for carcinoma of the biliary tract. Gall bladder carcinoma can be recognized by a polypoid mass or focal thickening of the gall bladder wall.[16] Preoperative ultrasonographic evaluation can more readily detect polypoid mucosal lesions of the gall bladder than flat lesions and those greater than 1 cm in diameter have been associated with malignancy.[17] Ultrasonography may detect advanced disease in upto 70% of the cases, but the sensitivity of trans-abdominal ultrasound in detecting early disease is variable.[17,18] A computed axial tomographic scan has often been used to show diffuse or focal gall bladder wall thickening and contrast enhancement of gall bladder wall in evaluating the patients with suspected malignancy as well as for small polypoid lesions of the gall bladder but it has not consistently been accurate in clearly identifying the gall bladder tumours in some studies.[19,20] Ultrasound guided fine needle aspiration cytology has about 95% diagnostic accuracy in evaluating of gall bladder masses and is considered a safe, rapid and accurate method for diagnosing gall bladder carcinoma.[21] Contrast enhanced ultrasonography has been used for the evaluation of gall bladder tumours at some centers.[22] Endoscopic ultrasonography and percutaneous transhepatic cholecystoscopy are also recent valuable tools for the detection and confirmation of early gall bladder carcinoma.[14,23] The pre-operative use of Cholangiography, Dynamic magnetic resonance imaging and Colour Doppler ultrasonography to differentiate benign from malignant disease has been associated with some degree of success.[24] Further refinements of these techniques may lead to better pre-operative detection of malignancy in the future.

Present era of laparoscopic cholecystectomy has given another dimension to this complicated issue. One must consider the possibility of tumour implantation at the laparoscopic port sites in the case of unsuspected gall bladder carcinoma during the operation.[5,7,25] Therefore, it is important to establish early detection and accurate staging of gall bladder carcinoma for the curative operation. This issue of laparoscopic cholecystectomy is not addressed in the current study as out of 16 cholecystectomies, only one was successfully completed laparoscopically whereas rest of the procedures were either performed by open technique or started laparoscopically and later converted to the open technique due to operative findings/problems.

The study concluded 1.15% patients had carcinoma gall bladder, of the total cases with gall bladder disease. More than 30% of the cases could not be diagnosed as gall bladder malignancy in the pre or intra-operative phase. Thus every specimen must be subjected to histopathological examination. Transabdominal sonography is not a definite method to diagnose carcinoma of gall bladder. In this study 75% cases were not detected by this investigation.

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