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The Occurrence of Gallbladder Carcinoma in Yemeni Patients Undergoing Cholecystectomy in Two Hospitals

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ABSTRACT

Background: Primary cancer of the gallbladder has wide geographical, ethnic and cultural variations with poor prognosis. Currently, there is no study about gallbladder carcinoma in Yemen.
The aim is to detect the occurrence of gallbladder carcinoma in Yemeni patients undergoing cholecystectomy.
Patients and Methods: A descriptive retrospective study of data of 940 patients operated for gallstones in two university hospitals in Yemen between 2002 and 2006 was carried out with respect to results of histopathological analysis of gallbladder specimens. There were 872 women and 68 men. Patients who have no histopathological reports in their files were excluded. Histopathological reports of 838 patients were retrospectively investigated for gallbladder malignancy.
Results: Gallbladder carcinoma was detected in 4 female patients of median age 66 years. No male patient was affected. Adenocarcinoma was the variety found in all four cases. All four patients with gallbladder cancer have history of longstanding gallstone disease.
Conclusion: The study supports the hypothesis that gallbladder carcinoma is rare and mostly affects elder women with long-standing gallbladder stones. The occurrence of gallbladder carcinoma in the targeted sample is significantly less than that of the western countries. Cooperation between surgeon, sonographist and histopathologist is strongly advised, particularly when gallbladder malignancy is suspected
Keywords: Cholecystectomy, Gallbladder, Cancer.

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INTRODUCTION

Primary cancer of the gallbladder was first described in 1777 by Maximillian DeStoll on the bases of two autopsies as a relatively uncommon tumor and a highly fatal disease (1). It is the most common malignancy of the biliary tract and the fifth common malignancy of gastrointestinal tract /GIT/(2, 3). Cancer of the gallbladder , despite its rarity, is known to vary greatly in incidence in different parts of the world and has also geographical, cultural and ethnic variations (1, 6).

It accounts for less than 1% of all incident of cancer in the USA, (4,5) and 1–2% of cholecystectomy specimens in the UK (4,5). The highest incidences are found in Native Americans and South Americans as well (7.5 per 100 000 for men and 23 per 100000 for women). However, the exact incidence of the disease in Yemen is still unknown.

Gall bladder (GB) cancer is primarily a disease of older women and has been associated with many risk factors including obesity, female gender, high parity among women, advanced age and ethnicity(2,5,6-14). The most common risk factor to gallbladder carcinoma development is longstanding gallstones, which cause chronic inflammation and chronic mechanical irritation in the wall of the gallbladder. This irritation maybe induced by time mucosal dysplasia, which may progress to cancer in situ eventually invasive carcinoma (2, 3, 7, 10). It is postulated that cancer of the gallbladder is associated with presence of longstanding gallstones in 75% to 90% of patients (1, 2). Since the incidence of gallbladder cancer in Yemen is still unknown and there is no enough information about it in the literature. This study attempts to detect the occurrence of this malignancy in Yemeni patients being operated in two university teaching hospitals between 2002 and 2006.

PATIENTS AND METHOD

Between 2002 and 2006 the researchers have performed 940 cholecystectomy for patients with gallbladder diseases particularly gallbladder stones with or without obstructive jaundice. The procedures were performed in two hospitals, Al-Kuwait University hospital in Sana'a and Al-Wahdah University hospital in Thamar. The group consists of 872 women and 68 men (92.8% and 7.2% respectively) at median age 38 years (ranging from 20 years to 78 years). All patients sent to Department of Surgery for cholecystectomy and were preoperatively diagnosed by sonographist who reported the presence of gallbladder stones with or without thickening of the gallbladder wall, in presence or absence of obstructive jaundice. An open cholecystectomy was performed for 192 patients, while laparoscopic cholecystectomy was performed for 748 patients. Gallbladder specimens were sent for histopathological analysis.

Out of 940 operated patients, 102 cases (96 women and 6 men) were excluded from the study because of absence of histopathological reports in their files.

A retrospective study of 838 patients (62 men and 776 women) whose histopathological reports were present in their files was conducted to detect the occurrence gallbladder cancer. Gall bladder histology is almost a standard postoperative procedure in Al-Kuwait University hospital especially for suspected cases.

RESULTS

Gallbladder carcinoma was detected only in 4 female patients (0.47%) from a series of 838 patients with median age 66 years (57, 60, 70 and 77 years). All four cases were associated

with gallbladder stones. Adenocarcinoma variety was found in all four cases. Diagnosis of the gallbladder cancer was made neither preoperatively by sonographist nor intraoperatively by the surgeon, but incidentally postoperatively by histopathologist. In one of the four cases, the diagnosis of malignancy was already suspected intraoperatively because of a gross thickening of gall bladder wall that enforced us to convert operation from laparoscopic to open. Data of patients with GB carcinoma are shown in (Table1). The indication for admission to the department of surgery for this case was calcular acute cholecystitis. The average age of patients with a gall bladder carcinoma was significantly higher i.e.66 years (ranges 57-77years) than the average age of patients with cholecystolithiasis without carcinoma i.e. 36 (range: 20-78 years) .

Jaundice was observed in 45 patients with gall bladder disease combined with obstruction of extrahepatic biliary tree. In 35 patients the diagnosis was calcular acute cholecystitis.

Acalcular acute cholecystitis was found in two patients despite these two cases were diagnosed preoperatively by ultrasound as calcular acute cholecystitis. Twenty three patients had hydrops of the gallbladder due to impacting stone in the neck of the gallbladder. Intraoperative findings of operated patients are shown in (Table 2).

Table (1): Data of patients with gallbladder carcinoma.

No.	Gender	Age	Weight	District	Clinical diagnosis	Intraoperative finding	Type of procedure
1.	female	57	70kg	Sana'a	Cal. cholecystitis	MGBS. No signs of malignancy	LCHCE
2.	female	60	55	Sana'a	Obstr. Jaund. (cholangitis)	MGBS & CBDS No signs of malig.	OCHCE
3.	female	70	65kg	Taiz	Cal. cholecystitis	SGBS&Thickened GB wall	Converted from LCHCE to OCHCE
4.	female	77kg	65kg	Sana'a	Cal. cholecystitis	MGBS	LCHCE

Cal.= calcular. Obstr. Jaund = obstructive Jaundice. MGBS= multiple gallbladder stones. GB= gallbladder CBDS= common bile stones. LCHCE= laparoscopic cholecystectomy. OCHCE= open cholecystectomy.

Table (2): Cholecystectomy, Intraoperative finding.

Operative finding	number of Patients	% of patients
Chronic cholecystitis	733	87.4%
Acute cholecystitis - calcular - acalcular	35 2	4% 0.2%
Hydrops	23	2.7%
Obstructive jaundice	45	5.3%
Total	838	100%

DISCUSSION

Cancer of the gallbladder is a fatal and rare malignant tumor with non-specific presentation and incidence of 1-2% (1, 3, 4). It is the most common malignancy of biliary tract and the fifth most common malignancy of GIT (2, 3). Gallbladder cancer is associated with many risk factors including the obesity, female gender, high parity among women, advanced age and ethnicity (2, 3, 6).Longstanding gallstones remain the most common risk factor to

gallbladder carcinoma development (2, 3, 7, 12).

Our goal is to detect the occurrence of the gallbladder carcinoma among Yemeni patients since this rare malignancy usually has wide geographical, ethnic and cultural variations (2, 11) and there are no reports in the literature or in Medline website about the incidence in Yemen. The histopathological reports of 838 patients operated for gallstones have been retrospectively investigated for primary gallbladder malignancy. Gallbladder carcinoma was detected in 4 female patients with incidence of 0.47%. This ratio remains lower if compared with that reported by Saneejv et al (3). High incidences are seen in Native Americans, South Americans and in North India (7.5 per 100000 for men and 23 per 100000 for women). Rates of up to 5 per 100000 are seen in Japanese and Hispanic American countries. Lower incidence was seen in USA, Nigeria and Singapore (3). However; in Chile, the cancer of the gallbladder is the most frequent cause of cancers related death (2, 3).

In the literature the majority of reports suggests that cancer of the gallbladder affects women two to six times more than men and the incidence peaks in the seventh decade of age (2). In our study, we found that all patients with cancer of the gallbladder were women. The absence of men to have carcinoma of GB in this study might be attributed to the small number of men included in the study. The age of affected women was in 6th and 7th decade of life which is consistent with the literature. The high incidence of GB cancer in elder patients might be attributed to the longstanding mechanical irritation of the mucosa of GB wall by gallstones. This repeated irritation of mucosa may induce mucosal dysplasia, which may progress to cancer in situ eventually invasive carcinoma (2, 3, 9).

Adenocarcinoma represents gallbladder malignancies in more than 87%, and then comes mixed adeno-squamous and squamous cell carcinoma (1, 2, 3) . In our cases, the only adenocarcinoma variety was detected. We attributed this finding to the small number of patients with gallbladder carcinoma.

The relationship between gallbladder stones and gallbladder cancer has been well established. Gallstones are found in 75-90% of patients with gallbladder carcinoma, while only 1% of patients with gallstones have cancer of the gallbladder (2, 3, 6, 9).This was confirmed in our series of patients where gallbladder carcinoma cases were associated with gallstones.

Large or multiple gallstones filling the gallbladder lumen may well constitute a marker for malignancy over time by possible repeated mechanical irritation of the gall bladder mucosa that may induce mucosal dysplasia, which may progress to cancer in situ eventually invasive carcinoma (2, 3, 10). This mechanism has been postulated by Solan and Jackson(10), that supports the findings of Lowenfells et al.(11) as well as Diehl et al.(12) who reported that gallstone size increases the risk of gall bladder carcinoma. However Moerman et al.(13) denied these findings and claimed that there is no relationship between stone size and gallbladder carcinoma development (13). In our sample, one patient has had solitary stone with unknown size, two patients have had multiple stones and the fourth case has had multiple stone combined with stones in CBD.

It is postulated that dysplasia is more likely to be found in patients with asymptomatic gallstones due to repeated mechanical irritation of the mucosa of gallbladder over a longer period of time, while symptomatic gallstones do not allow enough time for dysplasia to develop (6).

The occurrence of porcelain gallbladder is rare among biliary diseases but has strong association with gallbladder carcinoma (2, 6, 14). However; we did not detect porcelain

gallbladder in this study.

Despite the advances in hepatobiliary imaging techniques, the preoperative diagnosis of gallbladder cancer remains a challenging task because of the disease's non-specific presentation on one hand and lack of experienced sonographist, who usually seeks for stones rather than cancer of the gallbladder, on the other hand. Although the diagnostic accuracy of ultrasonography and computer tomography (CT) is more than 80% (3), the most common comment of findings described for gallbladder cancer is “diffuse thickening of the wall of the gallbladder". However, this is commonly reported for inflammatory conditions of the gallbladder and therefore does not aid in the cancer diagnosis (1). In our series, the preoperative sonographic comment for finding was either “normal wall thickening or mildly thickened gallbladder wall”. It is a rarity that Sonographist identifies a polyp or adenomyomatosis of the gallbladder preoperatively. Therefore the diagnosis of gallbladder cancer in our patients was made neither preoperatively nor intraoperatively but postoperatively by a histopathologist. This defect in experience of our sonographists is apparent in two cases with acalcular cholecystitis that were wrongly diagnosed preoperatively by sonographist as calcular cholecystitis.

The small number of patients with positive histopathological reports for GB malignancy (4 cases of 838) does not necessarily reflect the exact number of patients with cancer of gallbladder among Yemeni patients, because of two reasons:

1. Sometimes, pathologists do not actively look for dysplasia, which may be present in some cases.
2. The histopathological analysis of GB specimens is not a standard measure in all Yemeni hospitals. Therefore, further a larger scale study in other hospitals with use of histopathological analysis of gallbladder specimens as standard investigation, is advisable.

CONCLUSION

The present study supports previous reports that postulated that carcinoma of the gallbladder is rare and age-dependent malignancy and in most affects older women with long-standing gallstone disease. It appears that the occurrence of gallbladder malignancy in Yemeni patients is significantly less than that found among western people (0. 47 %, 1-2% respectively).

The cooperation between surgeon, sonographist and pathologist is recommended in order to diagnose gallbladder malignancy before surgical intervention. Further study in larger scale in other hospitals, where the use of histopathological analysis of gallbladder specimens is standard investigation, is advised.

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ظهور سرطان المرارة بين المرضى اليمنيين الذين خضعوا لعملية إزالة المرارة في مستشفيين

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ملخص

يوصف سرطان المرارة بأنه خبيث جدا وأن ظهوره يتنوع طبقا للمتغيرات الجغرافية والعرقية والثقافية. ولأننا لم نعثر على أي دراسات تعنى بسرطان المرارة عند المرضى اليمنيين فإن الهدف من خلال هذه الدراسة هو تتبع ظهور هذا السرطان عند المرضى اليمنيين الذين خضعوا لعملية إزالة المرارة

المرضى وطريقة إجراء الدراسة: أجرينا دراسة وصفية لملفات 940 حالة مرضية(872 إناث و 68 ذكور) كلهم خضعوا لعملية إزالة المرارة في مستشفيين جامعيين في الفترة من 2002 وحتى 2006 ، مركزين على نتائج تحاليل فحص الأنسجة للمرارات. من هذا العدد تم استبعاد الملفات التي لا تحتوي على نتائج للفحص النسيجي للمرارة(102ملفا). إذن 838 حالة هي التي تم دراستها بهدف التعرف على ظهور سرطان المرارة.

النتائج: ظهر سرطان المرارة عند 4 حالات كلها إناث وبمعدل عمر عند 66 عاما، جميعها كانت تعاني من آلام حصوات المرارة لفترات طويلة.

الموجز: لقد أكدت هذه الدراسة على الفرضية السائدة والتي ترى في سرطان المرارة بأنه مرض نادر يصيب كبار السن من الإناث وبالذات اللاتي يعانين من آلام حصوات المرارة لفترات طويلة ومزمنة. كما إن ظهور سرطان المرارة في العينة المستهدفة بالدراسة يعتبر أقل بكثير مقارنة بالبلدان الغربية.

ومن أجل تشخيص سرطان المرارة قبل إجراء العملية فإننا ننصح بالتعاون الوثيق بين الجراح وأخصائي الأشعة واختصاصي فحص الأنسجة خصوصا في الحالات المحتمل إصابتها بسرطان المرارة.

الكلمات الرئيسة: المرارة - عملية إزالة المرارة – سرطان المرارة.