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Abdul Shakor Shirpor
Department of Abdominal Surgery, Ali Abad Teaching Hospital, Kabul University of Medical Sciences, Kabul Afghanistan

Ahmad Amiri
Department of Abdominal Surgery, Ali Abad Teaching Hospital, Kabul University of Medical Sciences, Kabul Afghanistan

Mohammad Yusuf Yadgari
Department of Forensic Medicine, Kabul University of Medical Sciences, Kabul – Afghanistan

Mohammad Ibrahim Kamal
Department of Pathology, Ali Abad Teaching Hospital Kabul University of Medical Sciences, Kabul Afghanistan

Sultan Ahmad Halimi
Ph.D., Department of Pathology, Ali Abad Teaching Hospital Kabul University of Medical Sciences, Kabul Afghanistan

Corresponding Author:
Sultan Ahmad Halimi
Ph.D., Department of Pathology, Ali Abad Teaching Hospital Kabul University of Medical Sciences, Kabul Afghanistan

Incidental gallbladder carcinoma in patient's undergone elective cholecystectomy for lithiatic cholecystitis

Abdul Shakor Shirpor, Ahmad Amiri, Mohammad Yusuf Yadgari, Mohammad Ibrahim Kamal and Sultan Ahmad Halimi

Abstract
Background: Gallstone disease is a common surgical problem in all over the world and also in Afghanistan requiring cholecystectomy. It is known to produce diverse histopathological change in the gallbladder ranging from acute or chronic inflammation to metaplasia, dysplasia and even carcinoma.
An increasing frequency of gallbladder carcinoma has been observed during the last decade. The aim of this study is to find the premalignant lesions as well as incidental carcinoma in gallbladder resected for lithiatic cholecystitis. We focused mainly to determine the value of routine histopathologic examination of the gallbladder specimen resected for lithiatic cholecystitis.
Method: Total number of 250 consecutive patients with lithiatic cholecystitis who admitted for cholecystectomy at Ali Abad Teaching Hospital were included in this study. Laparoscopic cholecystectomy has been performed in 226 patients (90.4% of cases) while open surgery was performed in 24 (9.6%) of the patients. All resected gall bladders were sent to department of Pathology at Kabul University of Medical Science.
Result: Over a period of 3 years 250 patients with symptomatic gallstone were admitted for cholecystectomy at Ali Abad Teaching Hospital. Of these 250 cases, 180 were female (72%) and 70 were male (28%).
Majority of patients were between the ages of 31- 50 year (75%). Most common pathology noted in our study was chronic cholecystitis in 90% of cases (n=230). The most common benign lesions were Cholesterolosis in 80% (n=200) of cases followed acute cholecystitis in 10% (n=25), porcelain gall bladder (n=3), xanthogranulomatous cholecystitis (n=3). Incidental carcinoma was found in 4 patients (1.6%). Precursor lesions such as Antral metaplasia found in 8 (3.2%), dysplasia in 3(1.2%).
Conclusion: Our study emphasize that cholecystectomy performed for a common condition like gallstone disease can result in a diverse and wide spectrum of histopathological lesions ranging from benign to unexpected gallbladder carcinoma. The histopathology spectrum of gall bladder is extremely variable. Incidental diagnosis of carcinoma of gall bladder is not rare. If protocol of routine histopathology of gall bladder specimen is not followed sub clinical malignancy would be missed to be identified with disastrous result. We recommended routine histopathology of all gallbladder specimen.

Keywords: gall bladder, malignancy, cholecystectomy, cholelithiasis, chronic cholecystitis

Introductions

Gall stone disease accounts for the most common biliary tract disease in all over the world figuring to almost 12% of the population in United States and 18.5% in the Europe [1]. The majority of patients harboring gall stones through asymptomatic still carry a risk of developing complication [2]. Laparoscopic cholecystectomy (LC) regard the gold standard, being a very common modality of treatment is undergoing rapid improvement with the advent of newer technologies [3, 4].

The wide spread use of laparoscopic technique has led to an increased in referral for cholecystectomy. As a consequence, the incidental finding of gallbladder carcinoma (GBC) at an earlier stage has altered the management and the outcome of the disease. However, GBC remain a lethal disease associated with a dismal prognosis [5]. Incidental GBC is more likely be found in patient when age is more than 50, with dilated Bile ducts and gall bladder wall thickness. Surgeon to be more careful not to perforate the gall bladder during laparoscopic approach [6]. Preoperative predictors of incidental GBC have been poorly defined despite the frequency which cholecystectomy is performed [7]. The frequency of incidental gall bladder cancer has been reported to vary up to 2.85% [23, 17].

Chronic cholecystitis is not uncommon in our population due to gallstone and the best modality of treatment is laparoscopic cholecystectomy for those patient. As mentioned above, although rare, but the GBC is a deadly cancer of the biliary tract and if not diagnosed and treated in time, it has a worse prognosis of all cancers. Moreover, the lack of suspicion before the surgery and spillage of bile during LC has also made prognosis worse for patient who are incidentally diagnosis with GBC after LC.

Material and Methods

A total of 250 cholecystectomy cases were reviewed from January 2017 to August 2021. Of the 250 cases received, cholecystectomy specimens with a clinical diagnosis of benign gallbladder disease were included in the study. All patients presenting to OPD first and then admitted for cholecystectomy. The age category of patients with clinical diagnoses of chronic lithiatic cholecystitis were between 14 -70. Chronic cholecystitis was diagnosed in patient with history of pain in the right hypochandrium of more than 6 months' mild tenderness in the right hypochandrium (on clinical examination) and ultrasound showing thick wall of gall bladder with gallstones.

Laparoscopic and open cholecystectomy were performed by Dr. Abdul. Shakor (Shirpor) and his team under the standard protocol

The excised specimen was fixed in 10% neutral buffered formalin and sent for histopathological examination. Gallbladder wall more than 3 mm was considered to be thickened. Diagnosis of each case was confirmed on hematoxylin- and eosin-stained, formalin-fixed, paraffin-embedded sections. Microscopic findings such evidence of acute and chronic inflammation, and lesions such as hyperplasia, metaplasia, dysplasia and incidental carcinoma has been recorded. The medical records and clinical details of diagnosed cases of incidental gallbladder carcinoma including demographic data, clinical presentation, preoperative imaging findings such as ultrasound, and macroscopic features were reviewed.

Patients under the age of 14, and those who have clinically and grossly evident mass in gallbladder, those with traumatic rupture of gall bladder and choledocholithiasis were excluded from the study.

The main objective of the study was to find out the incidence of incidental gallbladder carcinoma and to review the risk factors associated with it. Hence, no control group has been taken and no statistical method has been applied for comparison with other studies.

Ethics and safety consideration

There was no any corporeal, mental and financial harm for the patients. Our research plan was initially approved by the ethical board of research committee at the Kabul University of Medical Sciences. The formal approval letter is available. We received no financial support for performing this research. The authors have no conflict of interest to declare.

Result

Over a period of 3 years 250 patients with symptomatic gall stone were admitted for cholecystectomy at Ali Abad Teaching Hospital. Of these 250 cases consist of 72% (181/250) female and 28% (69/250) male. Majority of patients were between the ages of 31- 50 year (65%). Most common pathology noted in our study was chronic cholecystitis seen in 90% of Cases (230/250). The most common benign lesions we found was Cholesterolosis in over 80% (200/250). Acute cholecystitis (25/250), Porcelain gallbladder (3/250), Xanthogranulomatous cholecystitis (3/250), and gallbladder polyp (3/250) were found respectively.

We found incidental carcinoma in 4 patients with no preoperative clinical presentation. The tumor was adenocarcinomas and even a single case with lymphomatous involvement. We additionally found other precursor lesions such as antral type epithelial metaplasia in 8 (3.2%), and dysplastic epithelium in 3 (1.2%) of our cases.

Clinical data of patients with incidental carcinoma

Clinical data of patients with incidental carcinoma					
Age and Sex	**Clinical features**	**Ultrasound findings**	**Preoperative diagnosis**	**Preoperative findings**	**Histopathology report**
60/F	Pain	Single Stone (20x12mm)	Chronic Cholecystitis	Wall thickness	Noninvasive adenocarcinoma well differentiated
58/F	Pain	Single stone (17x12mm)	Chronic Cholecystitis	Wall thickness	Noninvasive adenocarcinoma
48/F	Pain	Single stone (25x18mm)	Chronic Cholecystitis	Wall thickness	Noninvasive adenocarcinoma
45/M	Pain	Multiple stone	Chronic Cholecystitis	No suspicious lesion	Adenocarcinoma non invasive

Discussion

Total 250 patients with lithiatic cholecystitis operated for cholecystectomy were studied during January 2017 to August 2021 period. The age of patients with gallbladder disease ranged from 14 yrs to 80 yrs and were most commonly found in the 4th and 5th decades (188/250 cases, 75%). There were 70 males and 180 females with M: F ratio of 1:2.57. Out of 250 cases, 246 were benign gallbladder disease and 4 were neoplastic lesions of gallbladder on histopathological examination. The age of patients with malignancy varied from 48yrs to 60yrs. Malignancy was also more frequently encountered in females (3/4, 75%). Among the benign conditions detected in histopathological examination chronic cholecystitis was most commonly encountered (80% cases). Chronic cholecystitis was frequently associated with mucosal ulceration and Rokitansky Aschoff's sinus followed by cholesterolosis and Antral metaplasia. Mittal *et al.* [15] had similar findings; they found 77% cases of chronic cholecystitis. Other than chronic cholecystitis routine histopathological examination found, acute cholecystitis, (10%), Xanthogranulomatous cholecystitis (1.2%) in this study. Out of the 4 cases of incidentally diagnosed gallbladder malignancy, all cases were in situ adenocarcinoma and there was no invasive adenocarcinoma in extensive sectioning. Silk *et al.* [16] and Ataur *et al.* [19] found 100% cases of adenocarcinoma in their studies. Gallbladder malignancy is a rare entity, however, is common in the gastrointestinal tract and particularly observed in women from Chile, Japan, Northern India and Pakistan. The etiology of this malignancy is

complex but there is strong association with gallstones. Most are diagnosed at advanced stage with dismal prognosis having 5years survival rate of less than 5.0%. Detection at early stage has excellent prognosis increasing up to 90 - 100% 5years survival rate [20]. However, early detection is not possible due to delayed onset of symptoms or is masked off by chronic cholecystitis and is usually detected after simple cholecystectomy as incidental finding.

In this study the incidence rate of incidental GB carcinoma in routine post-cholecystectomy cases was 1.6%. Amanullah *et al.* (1.8%) and Shrestha *et al.* (1.4%) have found the incidence similar to ours whereas Khoo JJ &Nurul reports rate of incidental carcinoma to be 0.62%. Tantia *et al.*, Mittal *et al.* studied incidental gallbladder cancer in India and their rate of incidence were 0.6%, 0.99%, respectively. Daphna *et al.* observed 0.3% incidence, Zhang WJ *et al.* has shown its occurrence as low as 0.19%. It was even higher as shown by Shigeki *et al.*, finding incidence of incidental gall bladder cancer to be 4.7% and Navqi *et al.* has found its occurrence as high as 5.9% [18-21, 15].

The variety in the incidence may be due to inadequate preoperative evaluation or less number of cholecystectomy used for the study purpose. This is because the incidence of primary carcinoma of the gall bladder is itself low and hence finding of incidental carcinoma would be low too. Different incidence rates may also be attributed to different ethnic group, race and religion. The higher incidence of overall gallbladder disease in females (three times more in this study) explains the more frequent occurrence of GB malignancy in them. In contrast to benign diseases, malignancies were found to increase with increasing age. Chronic irritation and inflammation of the gallbladder, which leads to mucosal dysplasia and subsequent carcinoma that takes a long duration for promotion of tumor proliferation and hence the occurrence of malignancy in the elderly age group. There is a regional variation in male to female ratio from 1:1.1 to 1:5.5 in the world literature. Female to male ratio is even high in those areas where the gallbladder disease and gallbladder carcinoma is rare. Only Smithies has presented a small series of carcinoma gallbladder which is more common in males than females [22].

In our series 75% were females and 25% were males with male to female ratio of 1:3 which is similar to regional and international studies. Since, the number of cholecystectomy cases in our study is much smaller compare to others, the incidence of incidental carcinoma might be higher if large series of patients consider. Gallbladder malignancy doesn't have a typical clinical feature and its usual presentation mimics that of benign gallbladder disease. Most of these patients presents with syndromes of acute or chronic cholecystitis [23] Skil *et al.* [16] reported that there were no identifiable symptoms of carcinoma gallbladder and duration of symptoms are variable in different patients. Pain is the most prevalent symptom (50%) as described by Wanebo [17]. In this study symptoms in majority of patients were abdominal pain, while some of the patients present with mild nausea, and vomiting. Out of 4 cases only in 2 cases (50%) ultrasound predicted thickened wall. Agarwal & Kapoor said in their literature that an irregular or localized thickening of the GB wall should be treated as 'suspected' gallbladder cancer and extended cholecystectomy should be done in those cases [25]. In those 4 cases of incidentally diagnosed gallbladder cancer, 3 patients (75% cases) had single large calculi and average diameter of the stones was 20 mm. It is a well-established fact that gall stone size is related to the risk of developing malignancy. Diehl first studied the relation of gallstone size and risk of gall bladder cancer in 1983 and suggested that the larger the gall stones (>2 cm in diameter), the greater the association with gall bladder carcinoma [27]. Different studies also support this fact [26]. It is a standard practice to perform routine histopathological examinations for all cholecystectomy specimens. Various studies including the working report of Royal College of Pathologists have recommended for that every gallbladder specimen should be examined, as significant pathology may be present with normal gross morphology [28]. Samad and Amanullah and also Shreshtha *et al.* shared the same strategy [29, 30]. Recently few other investigators have challenged this practice. They have suggested that all cases of GB carcinoma have some macroscopic features like thickened fibrotic wall, mucosal ulceration, nodular mucosa or polyploidy projections which can be used as a guide for sending for histopathology. Bazoua *et al.* observed that all gallbladder cancers had thickened fibrotic wall [31]. Different studies also showed similar observation that, abnormal macroscopic appearance were present either pre or intraoperatively in all cases of invasive carcinoma and thus recommended for selective policy rather than routine histological examination of non-fibrotic or thickened-wall gallbladder [31, 32]. This study showed that radiological and preoperative findings were not helpful in raising high index of suspicion in all the cases of incidental carcinomas. Preoperative diagnosis of malignancy was difficult and combined preoperative and intraoperative findings failed to detect malignant cases in this study. Macroscopic findings of all incidental carcinomas had thick wall gallbladder in those studies where selective histopathology examinations were recommended. However, this study showed thickened GB mucosa in 3 cases of incidental carcinomas and the remaining 1 had no suspicious lesion or any specific changes intraoperatively. While on gross, other than thickened GB, nonspecific mucosal changes such as, irregular, granular mucosa, mucosal ulceration, contracted GB were noted. Therefore, no specific clinical or macroscopic finding can be assigned to characterize incidental carcinoma pre or intraoperatively to have clinical suspicion of malignancy. Only histological examination remains the tool for the detection of occult malignancy. Authors who propose for selective policy of histological examination state that incidental carcinomas if found during histopathological examination would be at early stage and simple cholecystectomy performed for benign gallbladder disease would be sufficient enough in giving good clinical outcome [31]. For the management of early stage carcinoma, Vincenzo *et al.* [32] suggested more aggressive surgery, as there was improvement of survival rate in comparison to those treated with simple cholecystectomy. Similar view is shared by Mishra *et al.* [33] recommending re-resection for all disease except Stage IA, for patients whose cancer is an incidental finding on pathologic review. However, there is still a controversy regarding management of GB malignancy at stage T1. Decision upon further surgical management of the incidental carcinomas thus depends upon the stage after pathological examination as well as, patient's fitness for re-surgery. Routine histological examination of all gallbladder specimen is therefore well justified as finding of incidental

carcinoma might alter the management and thus the clinical outcome.

Conclusion

Our findings concluded that although primary carcinoma of the gallbladder is known for late presentation and poor prognosis, occult carcinoma of gallbladder detected incidentally only by histopathological examination of post-cholecystectomy specimen at earlier stages and thus should have better prognosis. Our result also clarifies that protocol of routine histopathological examination of gallbladder has to be applied in all gallbladder specimen resected for lithiatic cholecystitis.

Suggestion

1. Since occult Gallbladder carcinoma can be diagnosed incidentally only by histopathological examination, therefore we suggest microscopic examination of gallbladder as a routine tool that has to be performed in all cases of chronic lithiatic cholecystitis.
2. During laparoscopic cholecystectomy, when the gall bladder walls seems, that is thick and edematous, we need to be careful to avoid rupture of gall bladder and spillage of bile, therefore it's better to use endo bag to out gall bladder from abdominal cavity to avoid the probable spread of cancer cells.

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References

1. Jayasundara JA, de Silva WM. Histological assessment of cholecystectomy specimens performed for symptomatic cholelithiasis: Routine or selective? Ann R Coll Surg Engl. 2013;95:317-22.
2. Ramraje SN, Pawar VI. Routine histopathologic examination of two common surgical specimens-appendix and gallbladder: Is it a waste of expertise and hospital resources? Indian J Surg. 2014;76:127-30.
3. Siddiqui FG, Memon AA, Abro AH, Sasoli NA, Ahmad L. Routine histopathology of gallbladder after elective cholecystectomy for gallstones: Waste of resources or a justified act? BMC Surg. 2013;13:26.
4. Deng YL, Xiong XZ, Zhou Y, Shrestha A, Li FY, Cheng NS. Selective histology of cholecystectomy specimens - Is it justified? J Surg Res. 2015;193:196-201.
5. Taylor HW, Huang JK. 'Routine' pathological examination of the gallbladder is a futile exercise. Br J Surg. 1998;85:208-6.
6. Dix FP, Bruce IA, Krypcyzk A, Ravi S. A selective approach to histopathology of the gallbladder is justifiable. Surgeon. 2003;1:233-5.
7. Swank HA, Mulder IM, Hop WC, van de Vijver MJ, Lange JF, Bemelman WA. Routine histopathology for carcinoma in cholecystectomy specimens not evidence based: A systematic review. Surg Endosc. 2013;27:4439-48.
8. Basak F, Hasbahceci M, Canbak T, Sisik A, Acar A, Yucel M, *et al.* Incidental findings during routine pathological evaluation of gallbladder specimens: Review of 1,747 elective laparoscopic cholecystectomy cases. Ann R Coll Surg Engl. 2016;98:280-3.
9. Shrestha R, Tiwari M, Ranabhat SK, Aryal G, Rauniyar SK, ShresthaHG. Incidental gallbladder carcinoma: Value of routine histological examination of cholecystectomy specimens. Nepal Med Coll J 2010;12:90-4.
10. Lazcano-Ponce EC, Miquel JF, Muñoz N, Herrero R, Ferrecio C, Wistuba II, *et al.* Epidemiology and molecular pathology of gallbladder cancer. CA Cancer J Clin. 2001;51:349-64.
11. Pandey M, Shukla VK. Diet and gallbladder cancer: A case-control study. Eur J Cancer Prev. 2002;11:365-8.
12. Misra S, Chaturvedi A, Misra NC, Sharma ID. Carcinoma of the gallbladder. Lancet Oncol. 2003;4:167-76.
13. Kalita D, Pant L, Singh S, Jain G, Kudesia M, Gupta K, *et al* Impact of routine histopathological examination of gall bladder specimens on early detection of malignancy – A study of 4,115 cholecystectomy specimens. Asian Pac J Cancer Prev. 2013;14:3315-8
14. Grobmyer SR, Lieberman MD, Daly JM. Gallbladder cancer in the twentieth century: Single institution's experience. World J Surg. 2004;28:47-9
15. Solaini L, Sharma A, Watt J, Iosifidou S, Chin Aleong JA, Kocher HM. Predictive factors for incidental gallbladder dysplasia and carcinoma. J Surg Res. 2014;189:17-21.
16. Mittal R, Jesudason MR, Nayak S. Selective histopathology in cholecystectomy for gallstone disease. Indian J Gastroenterol. 2010;29:26-30.
17. Silk NY, Douglas JR, Nava HR *et al* Carcinoma of gallbladder. The Rosewell Park experience. Ann Surg. 1989;210:751.
18. Wanbeo HJ, Vejeridis MP. Treatment of gall bladder cancer. Cancer Treat Res. 1994;69: 97-109.
19. Daphna W, Mehrdad H, Noa BJ, Sandbanand AH. Incidental finding of gallbladder carcinoma. Israel Med Assoc. J. 2002;4:334-6
20. Ataur R, Syed MA, Nadeem K, Attaullah AA, Muzaffar US. Frequency of Carcinoma Gallbladder in patients undergoing surgery for chronic Cholecystitis with Cholelithiasis. J Med Sci. 2006 Jan;14:26-9.
21. Lai CH, Lau WY. Gallbladder cancer; a comprehensive review. Surgeon. 2008;6:101-10.
22. Naqvi SQH, Mangi IH, Dahri FJ, Khaskheli QA, Akhund AA. Frequency of carcinoma of gall bladder in patients with cholelithiasis. Gomal Journal of Medical Sciences. 2005;3(2):41-3
23. Solan MJ, Jackson BT. Carcinoma of gallbladder: C1linical appraisal and review of 57 cases. Br J Surg. 1971;58:593-7.
24. Piehler JM, Crichlow RW. Primary carcinoma of gallbladder. Surg Gynecol Obstet. 1978;147;929- 42.
25. Shigeki Y, Yasuo A. Yoshiaki M *et al.* Occult gall bladder carcinoma after laparoscopic cholecytectomy: A report of four cases. J Nippon Med Sch. 2007;74:300-5.
26. Agrawal S, Kapoor VK. Thick walled gallbladder. Natl Med J India. 2006;19(1):37-8.
27. Lowenfels AB, Walker AM, Althaus DP, Townsend G, Domellöf L. Gallstone growth, size, and risk of

gallbladder cancer: an interracial study. Int J Epidemiol. 1989;18:50-4.
28. Diehl AK. Gallstone size and the risk of gallbladder cancer. JAMA, 1983, 2
29. Royal College of Pathologists. Histopathology of limited or no clinical value. Report of Working Group of the Royal College of Pathologists 2nd Ed., London, 2002.
30. Sherestha R, Tiwari M, Ranabhat SK, Aryal G, Rauniyar SK, Shrestha HG. Incidental gallbladder carcinoma: value of routine histological examination of cholecystectomy specimens. Nepal Med Coll J. 2010;12(2):90-4.
31. Amanullah MK, Rizwn AK, Shahid S, Veena M. Occult carcinoma of gallbladder: Incidence and role of simple cholecystectomy. JK- Practitioner 2007;14:22-3.
32. Bazoua G, Hamza N, Lazim T. Do we need histology for a normal-looking gallbladder? Surgeon. 2003;1:233-5.
33. Vincenzo C, Enrico F, Cristina P *et al.* Early gallbladder carcinoma: A single-center experience. Tumori. 2006;92:487-90.
34. Misra S, Chaturvedi A, Misra NC, Sharma ID. Carcinoma of the gallbladder. Lancet Oncol. 2003;4:167-76.