Incidental gallbladder cancer at cholecystectomy



Ann. Ital. Chir., 2017 88, 5: 399-402 pii: S0003469X17026665

Faik Tatli*, Abdullah Ozgönül*, Yusuf Yucel*, Hüseyin Cahit Yalçin*, Reşit Çiftçi*, Mehmet Gümer*, Firat Erkmen*, Rabia Altuntaş**, Ali Uzunköy*

*Harran University, Faculty of Medicine, General Surgery, Şanlıurfa, Turkey

Incidental gallbladder cancer at cholecystectomy

BACKGROUND: Gallbladder tumours rank fifth in the world among gastrointestinal system tumours. Coincidental gall-bladder tumours are diagnosed during cholecystectomies, or by examining the cholecystectomy material.

AIMS: In this study, we aimed to evaluate the incidence of gallbladder cancer among patients undergoing cholecystectomies due to gallbladder disease.

STUDY DESIGN: Retrospective study

METHODS: The files of 341 patients who had undergone routine cholecystectomy operations between January 2013 and March 2016 were reviewed, and their pathology results were recorded. Those patients with gallbladder carcinomas were evaluated in terms of age, gender, preoperative findings, existing symptoms, radiological findings, surgical findings and follow-up. The cancer invasion depth was classified according to the American Joint Commission on Cancer (AJCC) atlas, and this study was approved by the ethical committee of our university.

RESULTS: Among the 341 patients who participated in this study, 253 (74.41%) were female, 88 (25.80%) were male, and their average age was 49.61 years old (17-86). Seven of the patients (2.05%) had gallbladder tumours; six of which were female, one was male and their average age was 67.71 years old (62-76). One tumour was diagnosed as a frozen specimen during the operation, while the others were diagnosed during the postoperation phase. Three of the patients had T1b and four had T2 tumours.

CONCLUSION: Gallbladder tumours detected incidentally could extend survival rates with proper surgical intervention and chemotherapy. The possibility of a tumour should not be dismissed in those patients with advanced age, females or patients with gallbladder stones. Frozen specimens should be created during a cholecystectomy, and if there is any doubt about the diagnosis, a postoperative histopathological examination of the gallbladder should be conducted.

KEY WORDS: Cholecystectomy, Gall bladder stone, Incidental gallbladder carcinoma

Introduction

Gallbladder tumours rank 5th worldwide among gastrointestinal system tumours, and they are the most frequently found tumour of the biliary system ¹.

Pervenuto in Redazione Novembre 2016. Accettato per la pubblicazione Gennaio 2017.

Correspondence to: Faik Tatli, Prof. Assist Harran University, Medical Faculty Department of General Surgery, 63100, Sanliurfa, Turkey, (e-mail: faiktatli-@hotmail.com)

Approximately 90% of gallbladder tumours are accompanied by gallbladder tumors ², since gallbladder stones and chronic inflammation are common risk factors for gallbladder tumours ³ Most gallbladder tumours are detected during cholecystectomies for gallbladder stones, and for benign cases, incidentally during the examination of the specimen after a cholecystectomy ⁴. Incidental gallbladder tumours were seen in approximately 0.1-3.3% of the cases in the literature ⁵⁻⁷.

In this study, we aimed to evaluate gallbladder cancer events among patients who had undergone cholecystectomies due to gallbladder disease.

^{**}Harran University, Faculty of Medicine, Department of Pathology, Şanlıurfa, Turkey

Materials and Methods

The files of 341 patients who had routine cholecystectomy operations between January 2013 and March 2016 were reviewed. The patients' ages, genders, preoperative symptoms (pain in the epigastric region, dyspepsia, nausea/vomiting, right upper quadrant pain or positive Murphy's sign), reasons for surgery (stone or polyp), operation types (open or laparoscopy) and histopathological results were noted.

The pathological results of the cases were examined, and seven (2.05%) patients with gallbladder carcinomas were evaluated in terms of age, gender, preoperative symptoms, laboratory/radiological findings, surgery type (open versus laparoscopic), reoperation due to gallbladder cancer and follow-up. The cancer invasion depths were classified according to the American Joint Commission on Cancer (AJCC) atlas. The T1 tumours were followed-up without surgery, while the T2 tumours were treated with segment IVb and V liver resections and lymph node dissections. The collected data was analysed using SPSS 16 for Windows (SPSS Inc., Chicago, Illinois, USA). Before data collection began, this study was approved by the ethical committee of our hospital.

Table I - Sign and symptoms of all patients

Symptoms//signs	Frequency			
Pain in epigastria region	249(73.2%)			
Dyspepsia	218(64.1%)			
Nausea/Vomiting	165(48.5%)			
Right upper quadrant pain	90(26.4%)			
Murphy's sign positive	47(13.8%)			

Results

Among the 341 patients participating in this study, 253 (74.41%) were female and 88 (25.80%) were male. The average age was 49.6 years old (17-86). The majority of the events (99.4%) showed acute and chronic stone cholecystitis, while two (0.6%) underwent surgery due to polyps. Five of the patients had simultaneous choledocholithiasis, and two had Mirizzi syndrome type II. Forty-two patients (12.31%) had open operations and 299 patients (87.68%) had laparoscopic operations.

The patient complaints included epigastric pain (73.2%), dyspepsia (64.1%) and nausea/vomiting (48.5%) (Table I). Seven of the patients who had cholecystectomies due to gallbladder disease (2.05%) had gallbladder carcinoma. Six of these patients were female, one was male, and their average age was 67.7 years old (62-76). In all of the events, adenocarcinomas were detected histopathologically. Moreover, all of the patients with gallbladder carcinoma had gallbladder stones, and four of these patients had acute cholecystitis and wall thickness, with three having only cholelithiasis. The liver function tests of all of the patients were normal before their operations. The surgeries of two of the patients with gallbladder carcinoma were changed to open, and completed accordingly. One patient was diagnosed by a frozen section because the intraoperative view was consistent with malignancy. Three of the patients had T1b and four had T2 tumours. After diagnosing these four patients, liver resections (segments IVb and V) and lymph node dissections were conducted using an open surgical approach. All of the events were followed for an average of 16.6 months (Table II).

Table II - Clinical and histopathological findings of incidental gall bladder carcinoma, a American Joint Commission on Cancer

ID	Age	Sex	Ultrasonography	Operation Type	Intraoperative Findings	Pathology	Stage ^a	Tumor Location	Current Status
1	62	Female	Cholelithiasis Wall Thickened	Lap/ Elective	Cholelithiasis	Adeno Ca Wall Thickened	T1b Liver Metastasis	Corpus	Alive
2	76	Female	Cholelithiasis Elective	Lap Open Mirizzi	Adenosis	Adeno Ca	T2	Fundus	Alive
3	76	Male	Cholelithiasis Wall Thickened	Lap/Elective Wall Thickened	Cholelithiasis	Adeno C	Т2	Fundus	Alive
4	63	Female	Cholelithiasis	Lap/Elective	Cholelithiasis	Adeno Ca	T2	Corpus	Alive
5	58	Female	Cholelithiasis	Lap/Elective	Cholelithiasis	Adeno Ca	T1b	Corpus	Alive
6	74	Female	Cholelithiasis Wall Thickened	Lap Open Elective	Wall Thickened Adenosis	Adeno Ca	T1b	Corpus	Alive
7	65	Female	Cholelithiasis Wall Thickened	Lap/Elective	Wall Thickened	Adeno Ca	T2	Corpus	Alive

Discussion

Gall bladder tumours were first defined by De Stoll in 1777 (8). They are very rare, with a poor prognosis. Since the use of laparoscopy has become more widespread in the treatment of gallbladder diseases, the frequency of finding incidental gallbladder tumours has increased. Incidental gallbladder tumours were seen in approximately 0.1-3.3% of the cases in the literature (5,6,7). In this study, incidental gallbladder tumours were detected at a rate of 2.05%.

There is a high possibility that gallbladder tumours are correlated with gallbladder stones. All of the patients with gallbladder tumours in this study had gallbladder stones. A porcelain gallbladder, gallbladder adenomatous polyps, advanced age, female gender, chronic infection, exposure to carcinogenic substances and the existence of an abnormal pancreaticobiliary channel are also risk factors for gallbladder tumours ⁹. Adenoma of gallbladder are prevelant in women and association with gallstones was found in 62% of gallbladder adenoma ^{10,11}. In the series mentioned in the article by Spaziani E. et al., it is stated that surgery is proposed when gallbladder adenoma is associated with cholelithiasis in all cases because of the increased risk of malignancy development, independently from the dimension of the lesion ¹¹.

Gallbladder tumours are generally detected at advanced stages, and the prognosis is quite poor, with a 5-year life expectancy of approximately 5%. For an early diagnosis, the 5-year life expectancy is approximately 90-100% ^{12,13}. Those patients whose tumours are incidentally detected during cholecystectomies have the best prognoses ¹⁴. All of the events in this study were incidentally detected, and all the events were followed for an average of 16.6 months.

an average of 16.6 months. Surgery is the most effective treatment method for gall-bladder tumours, and the surgical approach depends on the invasion grade of the tumour ¹⁵⁻¹⁶. For tumours in situ and T1 stage tumours, a simple cholecystectomy is sufficient, but for T2 stage tumours, radical operations should be added to the cholecystectomy ¹⁷. Four T2 patients in our series had liver resections and lymph node dissections; however, no additional surgical interventions were applied to the other patients. One of our cases had metastasis, and no relapses or metastases were present in the other patients. The patient with metastasis (no: 1) rejected chemotherapy treatment during the postoperational period.

When examining patients with gallbladder tumours, these tumours have been seen more frequently in women and in advanced ages ¹⁸. In our study, six of the seven patients with incidental gallbladder tumours were female (85.71%), and their average age was 67.71 years old, which was older than the other patients in this study (67.7 versus 49.6 years old).

Many of the authors in the literature have argued that there could be port-site metastasis after a laparoscopic

cholecystectomy 19-20, depending on the invasion depth of the tumour, and the effusion of tumour cells during the removal of the gallbladder ²¹⁻²². Five events in our study were finalized by closed procedures, and two with open operations; however, no port-site metastases were seen in any of our cases throughout the follow-up period. Since gallbladder carcinomas have such a poor prognosis, those that are detected incidentally can extend the patient survival rates with proper surgical intervention and chemotherapy. The possibility of a tumour should be kept in mind when performing surgery on the elderly, females, patients with gall bladder stones and over adhesiveness during the operation. After a laparoscopic cholecystectomy all specimen should be opened and inspected. Frozen samples should be taken during cholecystectomies, and if there is any doubt about the diagnosis, a postoperative histopathological examination of the gallbladder should be performed.

Acknowledgements

The authors would like to thank all of the study participants involved in this investigation.

Riassunto

I tumori della colecisti occupano il Quinto posto nel mondo tra i tumori del sistema gastroenterico. Accidentalmente essi vengono diagnosticati durante una colecistectomia oppure all'esame anatomopatologico del pezzo anatomico. Lo scopo di questo studio retrospettivo è stato quello di valutare l'incidenza del cancro della colecisti nei pazienti sottoposti a colecistectomia per patologia della colecisti. Sono state sottoposte a revisione le cartelle cliniche di 341 pazienti sottoposti a colecistectomia tra il gennaio 2013 e il Marzo 2016, registrando i referti anatomo-patologici. Dei pazienti con carcinoma della colecisti sono state considerate l'età, il genere, gli esami preoperatori, la sintomatologia esistente, i referti radiologici, i reperti chirurgici ed il follow up.

La profondità di invasione carcinomatosa è stata classificata secondo la American Joint Commission on Cancer (AJCC) e lo studio è stato approvato dal comitato etico della nostra università.

Risultati: tra i 341 pazienti partecipanti allo studio 253 (74,41%) erano donne, 88 (25,80%) uomini, e l'età media era di 49,61 anni (range 17-86). Sette di questi pazienti (2,05%) avevano tumori della colecisti; sei di essi erano donne ed uno un uomo, dell'età media dii 67,71 anni (range 62-76). Un tumore è stato diagnosticato all'esame estemporaneo al congelatore durante l'intervento, mentre gli altri sono stati diagnosticati nella fase postoperatoria. Tre dei pazienti avevano tumori T1b e quattro T2.

In conclusion I tunori della colecisti diagnosticati accidentalmente possono aumentare l'incidenza della sopravviven-

za con trattamento chirurgico opportuno e chemioterapia. La possibilità di un tumore non dovrebbe essere trascurata in pazienti in età avanzata, di sesso femminile o in pazienti con calcolosi della colecisti. Durante l'intervento chirurgico dovrebbe essere effettuato l'esame estemporaneo al congelatore, e se c'è un dubbio circa la diagnosi dovrebbe essere effettuato l'esame istologico postoperatorio.

References

- 1. Jemal A, Siegel R, Ward E, et al: *Cancer statistics*. CA Cancer J Clin, 2006; 56:106-30.
- 2. Oddsdottir M, Hunter JG: Gall bladder and the extrahepatic billiary system. In: Brunicardi FC, Andersen DK, Billiar TR, Dunn DL, Hunter JG, Pollock RE(Eds): Schwartz's principle of surgery (8th ed.). New York: McGraw Hill, 2005; 1187-219.
- 3. Ghimire P, Yogi N, Shrestha BB: *Incidence of incidental carcinoma gall bladder in cases of routine cholecystectomy*. Kathmandu Univ Med J, 2011; 9:3-6.
- 4. Have PC, Simpson KJ, Garden OG: *Liver and biliary tract disease*. Hasle; C, Chilvers ER, Boon NA, Colldge NR (19th ed.). London: Churchill Livingstone. 831-88.
- 5. Zhang W, Xu G, Zou X, et al: *Incidental gallbladder carcinoma diagnosed during or after a laparoscopic cholecystectomy*. World J Surg, 2009; 33:2651-656.
- 6. Paliogiannis P, Scognamillo F, Attene F, et al: Preneoplastic and neoplastic gallbladder lesions accasionally discovered after elective video-cholecystectomy for benign disease. Ann Ital Chir, 2013; 84: 281-85.
- 7. Shrestha R, Tiwari M, Ranabhat SK, Aryal G, Rauniyar SK, Shresta HG: *Incidental Gallbladder carcinoma: value of routine histological examination of cholecystectomy specimens.* Nepal Med Coll J, 2010; 12:90-4.
- 8. De Stoll M: Rationis medendi in practice Unindobonensi. Part I Bernard, Vienna 1777.
- 9. Whang EE, Zinner MJ: Cancer of the Gall bladder and the bile ducts. In: Zinner MJ, Ashley SW, (eds). Maingot's abdominal operations (11th ed.). New York: McGraw Hill, 2007; 921-35.
- 10. Zani A, Pacilli M, Conforti A, et al.: Adenomyomatosis of the gallbladder in childhood: Report of a case and review of the literature. Pediatr Dev Pathol, 2005; 8:577-80.

- 11. Spaziani E, Di Filippo A, Picchio M, et al.: Prevalence of adenoma of gallbladder, ultrasonographic and histological assessment in a retrospective series of 450 cholecystectomy. Ann Ital Chir, 2013; 84: 159-64.
- 12. Eric CH, Lau WY: Gallbladder cancer, a comprehensive review. The surgeon, 2008; 10-9.
- 13. Misra MC, Guleria S: Management of cancer gallbladder found as a surprise on a resected gallbladder specimen. J Surg Oncol, 2006; 93: 690-8.
- 14. Contini S, Dalla valle R, Zinicola R: *Unexpected gallbladder cancer after laparoscopic cholecystectomy.* Surg Endosc 1999; 13: 264-67.
- 15. Whalen GF, Bird I, Tanski W et al: Laparoscopic cholecystectomy does not demonstrably decrease survival of patients with serendipitously treated gallbladder cancer. J Am Coll Surg, 2001; 192:189-95.
- 16. Muratore A, Polastri R, Capussotti L: Radical surgery for gall-bladder cancer: Current options. Eur J Surg Oncol, 2000; 26:438-43.
- 17. Kwon AH, Imamura A, Kitade H, Kamiyama Y: Unesuspected gallbladder cancer diagnosed during or after laparoscopic cholecystectomy. J Surg Oncol, 2008; 97:241-45.
- 18. Donohue JH, Andrew KS, Herman RM: *The national cancer database report on carcinoma of the gallbladder, 1989-1995.* Cancer, 1998; 83:2618-628.
- 19. Paolucci V: *Port-site recurrences after laparoscopic cholecystectomy*. J Hepatobiliary Pancreat Surg, 2001; 8:535-43
- 20. Sakata N, Suzuki M, Shibuya K, Takeda K, Matsuno S: Unexpected bile duct carcinoma presenting with port-site metastasis after laparoscopic cholecystectomy for cholecystolithiasis. J Hepatobiliary Pancreat Surg, 2002; 9:511-24.
- 21. Tsukada K, Hatakeyama K, Kurosaki I, et al.: Outcome of radical surgery for carcinoma of the gallbladder according to the TNM stage. Surgery, 1996; 120:816-21.
- 22. Johnson RC, Flingelstone LJ, Wheeler MH, Horgan K, Maughan TS: Laparoscopic cholecystectomy: Incidental carcinoma of the gallbladder with abdominal wall and axillary node metastasis. HPB Surg, 1997; 10:169-71.