International Journal of Biomedical Research

ISSN: 0976-9633 (Online)
Journal DOI:10.7439/ijbr
CODEN:IJBRFA

Research Article

The imperceivable fable of metamorphosis in 30 cases of gall bladder carcinomas, a study of 2 years

Shreesha Khandige, **Ragini Thapa*** and Suchithra Shetty

Department of Pathology, 2 Floor Academic Block Yenepoya Medical College, Derlakatte, Mangalore, Karnataka.575018

***Correspondence Info:**

Dr. Ragini Thapa, MD
Department of Pathology,
2 Floor Academic Block Yenepoya Medical College,
Deralakatte, Mangalore, Karnataka.575018
E-mail: ragpiyu2010@yahoo.com

Abstract

Amongst all hepatobiliary neoplastic lesions Gallbladder cancer is a highly aggressive malignancy that usually presents at an advanced, incurable stage.It is the fifth most common gastrointestinal tumor.A prospective study of 30 cases was carried out using routine and special histopathological methods for a period of 2 years. Out of the 30 cases studied majority of neoplasms were adenocarcinomas (80%), with female predominance (66%), followed by secondaries to gall bladder (10%). Squamous cell carcinoma and mucinous variant of gall bladder cancer still remains rare entity (3.33%) each. Intestinal type of adenocarcinoma though uncommon has male preponderance (3.33%).

Keywords: Neoplastic lesions, gall bladder

1. Introduction

Gallbladder cancer is a highly aggressive malignancythat usually presents at an advanced, incurable stage.1It is the fifth most common gastrointestinal tumor.2 Gallbladder cancer has propensity for early lymph node metastasis and direct invasion into the liver, as well as a remarkable tendency to seed the peritoneal cavity, biopsy tracts, and laparoscopic-port sites. Gallbladder cancer is occasionally diagnose incidentally on pathologic review of cholecystectomy specimens, and it may be in this population that appropriate surgical management has the most impact on long-term survival.

2. Materials and Methods

Present sudy was done on cholecystectomy specimens sent for histopathological evaluation to our department of pathology, other private nursing homes and hospitals in and around Mangalore during a period of 2 years (June 2011-September 2013). Grossing of the formalin fixed cholecystectomy specimens of gallbladder was doe. Required Sections of 5 microns thickness were cut and routinely stained with haematoxylin and eosin. Detailed analysis by light microscopy was done and recorded. Required clinical and imaging details were obtained for all the cases. Special stains were used wherever possible.

3. Results

Our study was carried out on a total of 30 cholecystectomy specimens received. The most common lesion of the gall bladder was adenocarcionomas of the gall bladder which constituted (80%) of all the neoplasms. (Table 1)

Table 1 showing frequency of various neoplastic gall bladder lesions

Histopathological diagnosis	No. of cases	Percentage
Adenocarcinoma	24	80%
Metastatic carcinoma	03	10%
Mucinous carcinoma	01	3.33%
Squamous cell carcinoma	01	3.33%
Intestinal type adenocarcinoma	01	3.33%

Table -2: Age and sex distribution of the patients in the cases studied

Diagnosis	Age	Male	Female
Adenocarcinoma	40-55yrs	05	19
Metastatic carcinoma	55-60 yrs	01	02
Mucinous carcinoma	45 yrs	00	01
Squamous cell carcinoma	55yrs	01	00
Intestinal type adenocarcinoma	50 yrs	01	00

Table 3:Grading of adenocarcinomas and corresponding frequency 137:

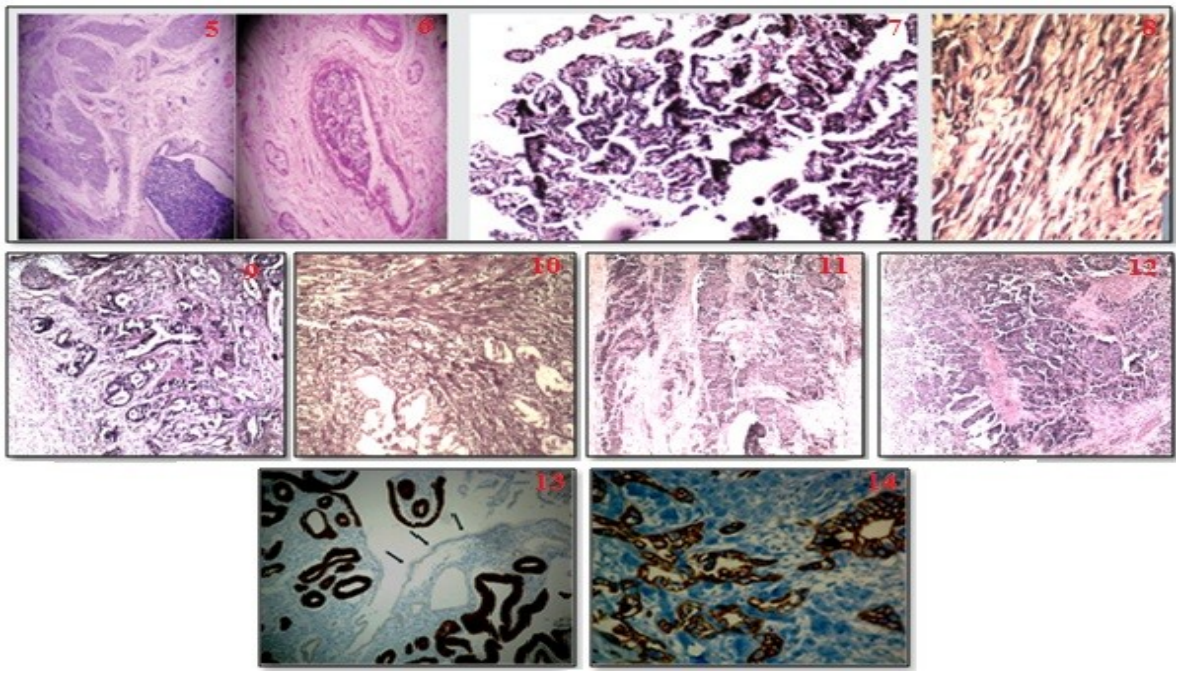
Grading	Percentage
Well differentiated	5/24 (20%)
Moderately differentiated	12/24(50 %)
Poorly differentiated	7/24(29%)

Mostly adenocarcinoma occur in 40 -55 yrs of age with female preponderance followed by secondaries that also have female preponderance. Fig(1-4), fig (9-12)

Maximum number of cases that were studied were moderately differentiated adenocarcinoma (50%) (fig9-12),fig(8),followed by poorly differentiated (29%)carcinomas. Cytokeratin expression is being frequently used for the differential diagnosis of carcinomas originating from different sites.[1] Among the various cytokeratins, the combination of cytokeratins (CKs) 7 and 20 /9 fig (13,14) is considered to be fruitful in differentiating primary hepatobiliary malignancies from secondaries.[1,2,20] The CK7+/CK20– immunoprofile of the normal gallbladder mucosa seems to be retained in early stage GBCs. Loss of this phenotype may be related to tumour progression.[2] A minority of GBCs is CK20-positive, representing perhaps an alternative pathway of carcinogenesis in the gallbladder through an intestinal phenotype.[3,4,5,20]

Fig 1-4: showing gross of gall bladder carcinoma.

Fig 5,6-tumor emboli from secondaries.fig 6-gall bladder carcinoma with deposits ovr colon and small bowel.fig 8-moderately differentiated adenocarcinoma.fig (9-12) adenocarcinoma gall bladder



4. Discussion

Carcinomas constitute exuberant majority of malignant tumors that arise in humans, metastasize to regional lymph nodes and then to other organs, such as the lungs, the brain, the liver, and the bones. Several times a malignant tumor presents itself to the patient, and the clinician by its manifestations at the metastatic site. Gallbladder cancer is a highly aggressive malignancy that manifests at an advanced, incurable stage.[6] It is the fifth most common gastrointestinal tumor.[7,8,9] Gallbladder cancer leads to early lymph node metastasis and direct invasion into the liver, has atendency to seed the peritoneal cavity, biopsy tracts, and laparoscopic-port sites. The median survival is less than 6 months after diagnosis. As is typical with solid gastrointestinal malignancies, chemotherapy has not had a significant impact on this tumor. Despite its aggressive nature, however, long-term cures have been reported after surgical resection, even with advanced locoregional disease. Gallbladder cancer is occasionally diagnosed incidentally on pathologic review of cholecystectomy specimens, and it may be in this population that appropriate surgical management has the most impact on long-term survival.

Pronounced geographic and racial differences exist in the frequency of this tumor.[7,8,9] High rates of gallbladder cancer are seen in South American countries, intermediate rates are observed in many European countries, and lower rates are observed in the United States, and theUnited Kingdom. In India urban areas show higher incidences than rural regions. Lower socioeconomic status may lead to delayed access to cholecystectomy for gallstones, which may increase gallbladder cancer rates.[10,11] Women are two to six times more commonly affected by gallbladder cancer than men, and the incidence steadily increases with age.[12,13] Other factors that increase the risk for gallbladder cancer include obesity, a high-carbohydrate diet, smoking,and alcohol .[14] The most significant risk factor for gallbladder cancer is the presence of a chronic inflammatory state of the gallbladder, usually as a result of gallstones. Most of the variance in geographic and racial gallbladder cancer rates can be explained by the varying incidence of gallstones in the populations. Gallbladder cancers can be categorized into infiltrative, nodular, combined nodular infiltrative, papillary, and combined papillary-infiltrative forms.[13,14], Infiltrated tumors cause thickening and induration of the gallbladder wall. Nodular types show early invasion through the gallbladder wall into the liver or neighboring structures and may be easier to surgically control than the infiltrative form. Papillary carcinomas have the best prognosis and exhibita polypoid cauliflower-like appearance. Histologically, the most common type of gallbladdercancer is adenocarcinoma. Other types, such as adenosquamous carcinoma, oat cell carcinoma,and sarcomas, have also been described. Rare primary histologies such as carcinoid, lymphoma, and melanoma have been reported. Adenocarcinomas can be divided subtypes, including well-differentiated,

papillary, intestinal type, pleomorphic giant cell, poorly differentiated small cell, signet ring cell, clear cell, colloid, and the choriocarcinoma-like cell subtype.[13,14,15,16] The papillary histologic subtype has the best prognosis whereas the poorly differentiated small cell tumor has the worst prognosis.[13,16] Nowadays gallbladder cancers have been divided into nonmetaplastic and metaplastic types on the basis of metaplastic changes in the tumor tissues. The metaplastic type showed a significantly improved survival rate.[15,16] Gallbladder cancers should be histologically graded from G1 (well differentiated) to G4 (undifferentiated).Papillary tumors are well differentiated and have an improved prognosis. The K-*ras* mutations was identified[16]and it is felt that allele-specific deletions of the p53, deleted incolon cancer (DCC), and 9p genes play an important role in the pathogenesis of gallbladder cancer. Gallbladder cancer can spread by direct invasionthrough the gallbladder wall into the liver or peritoneal cavity. The gallbladder has a narrow wall consisting of a thin lamina propria and a single muscle layer. If a gallbladder cancer penetrates this muscle layer, it has access to major lymphatic and vascular channels as well as the liver or peritoneal cavity by penetration through the wall. This may be the reason that gallbladder cancer seems to present in such advanced stages. Gallbladder cancer is an aggressive tumor that is highly lethal. While the overall 5-year survival reported in large reviews and surveillance programs is less than 5 percent, with a median survival of 5 to 8 months.[13,18,19]

References

1. Chang HJ, Kim SW, Lee BL, et al. Phenotypic alterations of mucins and cytokeratins during gallbladder carcinogenesis. *Pathol Int* 2004; 54: 576-584.
2. Duval JV, Savas L, Banner BF. Expression of cytokeratins 7 and 20 in carcinomas of the extrahepatic biliary tract, pancreas, and gallbladder. *Arch Pathol Lab Med* 2000; 124: 1196-1200.
3. Cabibi D, Licata A, Barresi E, et al. Expression of cytokeratin 7 and 20 in pathological conditions of the bile tract. *Pathol Res Pract* 2003; 199: 65-70.
4. Shimonishi T, Miyazaki K, Nakanuma Y. Cytokeratin profile relates to histological subtypes and intrahepatic location of intrahepatic cholangiocarcinoma and primary sites of metastaticadenocarcinoma of liver. *Histopathology* 2000; 37: 55-63.
5. Cooper DS, Schermer A, Sun TT. Classification of human epithelia and their neoplasms using monoclonal antibodies to keratins: strategies, applications, and limitations. *Lab Invest* 1985; 52: 243-256.
6. Perpetuo MO, Valdivieso M, Heilbrun LK, et al. Natural history study of gallbladder cancer: a review of 36 years experience at M.D. Anderson hospital and tumor institute. *Cancer* 1978;42:330–5.
7. Carriaga MT, Henson DE. Liver, gallbladder, extrahepatic bile ducts and pancreas. *Cancer* 1995;75 (1 Suppl):171–90.
8. Diehl AK. Epidemiology of gallbladder cancer: a synthesis of recent data. *J Natl Cancer Inst* 1980;65: 1209–10.
9. Serra I, Calvo A, Báez S, Yamamoto M. Risk factors for gallbladder cancer. An international collaborative case-control study. *Cancer* 1996;78:1515–6.
10. Nakayama F. Recent progress in the diagnosis and treatment of carcinoma of the gallbladder—introduction. *World J Surg* 1991;15:313–4.
11. Scott TE, Carroll M, Cogliano FD, et al. A case-control assessment of risk factors for gallbladder carcinoma. *Dig Dis Sci* 1999;44:1619–25.
12. Moerman CJ, Bueno-de-Mesquita HB. The epidemiology of gallbladder cancer: lifestyle related risk factors and limited surgical possibilities for prevention. *Hepatogastroenterology* 1999;46:1533–9.
13. Sumiyoshi K, Nagai E, Chijiiwa K, Nakayama F. Pathology of carcinoma of the gallbladder. *World J Surg* 1991;15:315–21.
14. Yamamoto M, Nakajo S, Tahara E. Carcinoma of the gallbladder: the correlation between histogenesis and prognosis. *Virchows Arch* 1989;414:83–90.
15. Wee A, Teh M, Raju GC. Clinical importance of p53 protein in gall bladder carcinoma and its precursor lesions. *J Clin Pathol* 1994;47:453–6.
16. Imai M, Hoshi T, Ogawa K. K-ras codon 12 mutations in biliary tract tumors detected by polymerase chain reaction denaturing gradient gel electrophoresis. *Cancer* 1994;73:2727–33.
17. Chow NH, Huang SM, Chan SH, et al. Significance of c-erbB-2 expression in normal and neoplastic epithelium of biliary tract. *Anticancer Res* 1995;15: 1055–9.
18. Cubertafond P, Gainant A, Cucchiaro G. Surgical treatment of 724 carcinomas of the gallbladder. Results of the French Surgical Association Survey. *Ann Surg* 1994;219:275–80.
19. Piehler JM, Crichlow RW. Primary carcinoma of the gallbladder. *Surg Gynecol Obstet* 1978;147:929–42.
20. Kalekou H, Miliaras D. Cytokeratin 7 and 20 Expression in Gallbladder Carcinoma. *Pol J Pathol* 2011; 1: 25–30.