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Neoplastic diseases of the gallbladder- a 5 year study

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Abstract

Introduction: Gallbladder diseases are the major causes of morbidity and mortality throughout the world. Majority of the diseases are related to gallstones. Gallstone disease is a risk factor for the development of gallbladder carcinoma.

Aims and Objectives: The objective is to study the morphological spectrum of neoplastic diseases in gallbladder, and to note the frequency of malignant neoplasms.

Materials and Method: The study was conducted on cholecystectomy specimens received in centrallaboratory, Department of Pathology, KIMS, Bengaluru from July 2009 to June 2014.

The cholecystectomy specimens received in 10% formalin were examined in detail for gross and microscopic changes. Neoplasms were studied and categorized.

Results: There were 700 cholecystectomy specimens received for histopathological study. There were 17 cases of neoplasms of which 6 were adenomas and 11 were carcinomas. Of the 11 carcinomas 3 were detected only on histopathological examination.

Conclusion: Histopathological examination of all the cholecystectomy specimens is a must to rule out incidental carcinoma.

Keywords: Adenoma, Gallbladder carcinoma, Adenocarcinoma gall bladder, Adenosquamous, Mucinous carcinoma.

Introduction

Diseases of gallbladder are one of the common causes of morbidity in the middle age and elderly. Majority of the diseases are related to gallstones. Gallstone diseases produce diverse histopathological changes in the gallbladder mucosa.(1)

Clinical description of biliary tract diseases appeared vividly in the writing of the ancient Indian physicians, Charaka (2nd century B.C) and Shushrutha (6th century B.C).(2)

Gallbladder carcinoma is the most common cancer of biliary tract and 5th most common gastrointestinal malignancy. It is characterised by rapid progression and very high mortality rate. Early stages of gallbladder carcinoma are usually asymptomatic or symptoms are very similar to those of benign conditions like chronic cholecystitis making it difficult for early detection. Detection at early stage leads to a good prognosis and prolonged survival. The incidence of gallbladder carcinoma varies by geographic, region and social ethnic group.(3)

Aim and Objectives

The objective is to study the morphological spectrum of neoplastic diseases in gallbladder, and to note the frequency and type of malignant neoplasms.

Materials and Method

Materials for this study were cholecystectomy specimens received in the Department of Pathology, Kempegowda Institute of Medical Sciences, Bengaluru from July 2009 to June 2014.

Gallbladder specimens were examined grossly for serosal and mucosal changes. The presence of calculus/calculi, number and type noted. The thickness of the wall was measured. In the presence of tumour, size, site, extent, colour and consistency was noted and bits taken. All cases reported as malignant or benign neoplasms were taken for the study.

Institutional ethical clearance was obtained.

Results

There were 17 cases of neoplasms detected in 700 cholecystectomy specimens studied. Six were benign and 11 were malignant neoplasms.

Five of six benign neoplasms were seen in females. Grossly these presented as smooth surfaced polyps (Fig. 1). These were tubular adenomas, one case showed pyloric and intestinal metaplasia.

Fig. 1: Gross photo showing benign polyp

Malignant neoplasms: There were 11 cases of carcinoma. Majority were seen in females (8 F and 3 M). The age ranged from 48 to 78 yrs. Grossly tumor was

seen in 5 cases (Fig. 2), remaining 6 cases showed irregular wall thickening. Gall stones were associated in 8 cases. Eight of 11 cases of carcinomas had preoperative diagnosis whereas, 3 were incidental carcinomas, as the diagnosis was done on histopathological examination.

Fig. 2: Gross photo showing infiltrating tumor in the fundus of gall bladder

Seven of 11 cases were associated with gall stones, multiple pigment stones were noted in 6 of 7 cases and one case had mixed stones.

Most common type of carcinoma was adenocarcinoma (9 cases) (Fig. 3).

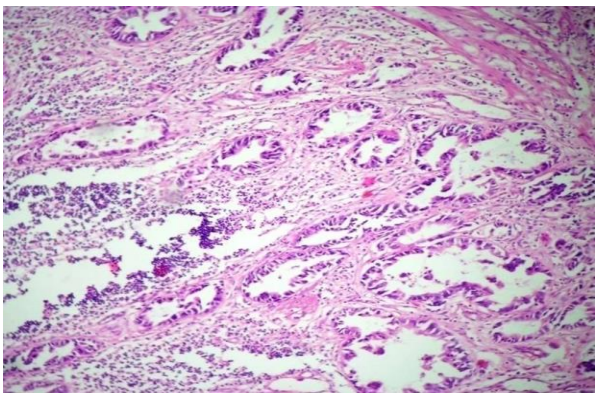
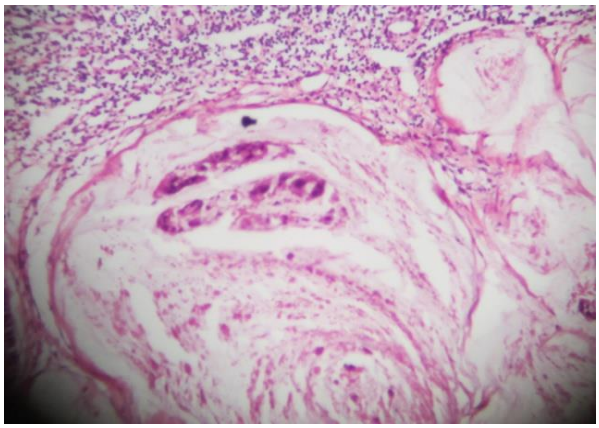


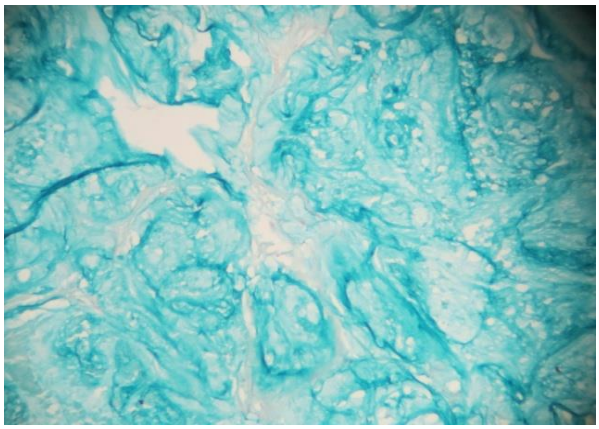
Fig. 3: Photomicrograph of well differentiated adenocarcinoma H&E x 100

One each of pure mucinous carcinoma and adenosquamous carcinoma were noted. Though 2 of the 9 adenocarcinomas showed mucinous differentiation, did not qualify for pure mucinous carcinoma as the tumor showed only 10% mucinous areas. Perineural and lympho vascular invasion were noted in 2 of 9 cases. One case showed direct infiltration into the liver bed.

Mucinous carcinoma: one case was diagnosed as mucinous carcinoma where the tumor showed >60% extracellular mucin with the tumor cells embedded in it (Fig. 4a). The mucin showed alcian blue (Fig. 4b) and PAS positivity.



a



b

Fig. 4a, b: Photomicrograph of mucinous carcinoma a: H&E x100, b: alcian blue x100

A case of adenosquamous carcinoma diagnosed showed both glandular and squamous components. The squamous component was more than 25% of the tumor and had many keratin pearls (Fig. 5). Metastasis to liver and lymphnode were also noted in the same case.

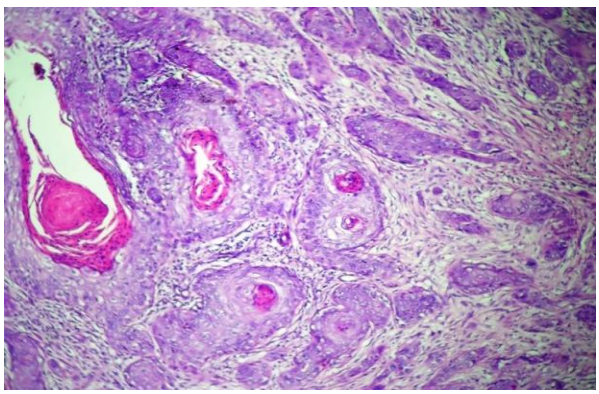


Fig. 5: Photomicrograph of adenosquamous carcinoma H&Ex100

Discussion

Diseases of gallbladder are one of the common causes of morbidity in the middle age and elderly.

Majority of the diseases are related to gallstones. Gallstone diseases produce diverse histopathological changes in the gallbladder mucosa.[1]

Neoplasms of gall bladder can be benign or malignant, most common being malignant.

Adenoma: Adenomas are benign tumors, may harbour foci of malignancy. These have to be studied carefully. We noticed 6 cases of adenomas in the gallbladder. None of them showed malignant change. Terada et al in their study of 540 cholecystectomy specimens found 7 cases of adenomas, which were of tubular type.**(4)** Mohan et al in their study found 2 cases of adenomas associated with stones.**(5)**

Carcinoma of gallbladder: Gallbladder carcinoma is the most common cancer of biliary tract and 5th most common gastrointestinal malignancy. It is characterised by rapid progression and very high mortality rate. Early stages of gallbladder carcinoma are usually asymptomatic or symptoms are very similar to those of benign conditions like chronic cholecystitis making it difficult for early detection. Detection at early stage leads to a good prognosis and prolonged survival. The incidence of gallbladder carcinoma varies by geographic, region and social ethnic group.[3]

First description of the gallbladder carcinoma was by Macmillan de stol in 1777.[6] Despite being first described more than two centuries ago in 1777, there has been little progress in the early diagnosis, prognosis and effective treatment. Carcinoma of the gallbladder is the most common malignant tumor of the biliary tract and is the fifth most mortality causing cancer and cases are alarmingly increasing in south east Asia.[7]

The highest figures are reported from the population of northern and eastern India, Japan, Chile, China, Eastern Europe, Native America and South America. It is not common in Europe and the United states. It is more frequent in Chile, Bolivia and Israel.[7]

The incidence of carcinoma of gallbladder in India ranges from 1.01 per 1 lakh for males to 10.1 per 1 lakh for females (ICMR) annual report of population based cancer registries of the National Cancer Registry Programme(1996), but the actual number may be more in the endemic zones of western Bihar and Eastern Uttar Pradesh where it is 3rd commonest malignancy of GI tract.[7]

The incidence is 10-12 times higher in northern India women as compared southern India. Incidence of GBC in northern India, 4.5/1 lakh for males and 10.1/1 lakh for females but low in South India,1.2/lakh and 0.9/1 lakh for males and females.[7]Probably it is attributed to the difference in the food habits between south Indians and north Indians.

Cholelithiasis is one of the major risk factors of GBC.

Seven of 11 cases of carcinoma had associated gall stones, most of them were multiple pigment stones.

Most of the carcinomas originate in the fundus(60%), about 30% in the body and 10% in the neck.[8,9]

Macroscopically most gallbladder carcinomas fall into one of the three categories: infiltrating, papillary and mucinous. The commonest is the infiltrating type, appears as diffuse thickening and induration of the gallbladder wall or infiltrating grey white mass.

The gallbladder may be distended by the tumor or collapsed due to obstruction of the neck or cystic duct. It can also assume an hourglass deformity when the tumor arises in the body and constricts the lateral walls. Papillary carcinomas are usually sessile and exhibit a polypoid or cauliflower like appearance. It may be localised usually in the fundus of the gallbladder but is more commonly seen as a solid fungating mass obliterating the lumen, necrosis and haemorrhage are common.[8,9] Mucinous and signet ring cell carcinomas have a mucoid or gelatinous cut surface. Spread over the peritoneum is a feature of many of these tumors and this may result in ascites.[8]

In the present study tumor was seen grossly in 5 cases, remaining 6 showed thickening of the wall, of which one had a gelatinous cut surface which was diagnosed as mucinous carcinoma by histopathology.

Adenocarcinoma is the commonest type of carcinoma occurring in the gall bladder. Most of them are infiltrating the entire wall. Perineural and lymphovascular invasion may be noted. The incidence of carcinomas in the present study is consistent with other studies.[4,5,10,11,12]

Most of the adenocarcinomas are well to moderately differentiate. They are composed of short or long tubular glands lined by cells that vary in height from low cuboidal to tall columnar cells. Mucin is frequently present. About one third of the well differentiated tumors show focal intestinal differentiation and contain goblet and endocrine cells. Adenocarcinomas may show cribriform or angiosarcomatous pattern. They may also contain cyto and synctiotrophoblast cells.[13]

About one fifth of adenocarcinomas are poorly differentiated and consists of masses or anastomosing strands of hyperchromatic cells with frequent mitosis and called as medullary type.[9]

Mucinous carcinomas constitute 2.5% of gallbladder carcinomas. They present with an acute cholecystitis type picture clinically. They are typically large and advanced tumors at the time of diagnosis and they exhibit more aggressive behaviour than do ordinary gallbladder carcinomas. Immunophenotypically they differ from conventional gallbladder adenocarcinomas by MUC2 positivity, from intestinal carcinoma by an often inverse CK7/20 profile, from pancreatic mucinous carcinoma by CDX2 negativity, and from mammary colloid carcinoma by a lack of MUC6.

Dursun et al in their study of 606 GBC found 15 mucinous carcinomas and noted male to female ratio 1:1 in contrast to conventional gallbladder carcinomas

which is more common in females. Tumor cells formed cribriform stellate clusters, largely within the centre of the mucin nodules in most of the cases. In other areas cells were lying individually within the mucin. Patients with mucinous carcinomas have worst prognosis.[14]

We noted a case of pure mucinous carcinoma in a female among the 11 carcinomas. Patient had presented clinically as acute cholecystitis.

Adenosquamous carcinoma of the gallbladder is a rare subtype of gallbladder cancer, characterized by a more rapid and invasive growth with infiltration of adjacent organs and less frequent lymphnode spreading when compared to adenocarcinoma.[15]We had a case of adenosquamous carcinoma in the present study.

Roa J C et al in their study of 606 carcinomas of gallbladder noted a high incidence of adenosquamous carcinomas (26%).[16]

Incidental carcinomas are carcinomas detected only on histopathological examination without any preoperative clinical diagnosis. We diagnosed 3 carcinomas on histopathological examinations which were not detected clinically and or by ultra sound examination. Two of these cases were diagnosed as acalculous cholecystitis and 1 case as calculous cholecystitis.

Some authors have reported high incidence of incidental carcinomas. Khan S.et. al,[10] reported 9 cases of adenocarcinoma which included 8 cases of incidental adenocarcinoma detected on histopathological examination. Stancu M et al[11] reported 32 cases of carcinomas, where only 9 cases had pre-operative diagnosis of gallbladder carcinoma. In the remaining 23 cases diagnosis was established after histopathological examination. Another study reported 20 malignant cases in 668 cholecystectomy specimens where preoperatively malignancy was suspected only in 6 cases.[12] Intra-operatively growth was observed in 10 cases, 9 cases were diagnosed by histopathological examination.

We had 3 cases of incidental carcinomas out of 700 cholecystectomies accounting to 0.43% similar to their findings.

Conclusion

Most of the gall bladder carcinomas are associated with gall stones, adenocarcinoma being the most common. Early diagnosis of gallbladder carcinoma is difficult as the patients may not have any symptoms or may present with symptoms of cholecystitis. Hence histopathological examination of all gallbladders removed is a must.

References

1. Baidya R, Sigdel B and Baidya NL. Histopathological changes in gallbladder mucosa associated with cholelithiasis. Journal of pathology of Nepal (2012) Vol. 2, 224-225.
2. Tandan R K. pathogenesis of gallstones in India. Tropical Gastroenterol 1988; vol 9(2): p82-93.
3. Diehl AK, (1983): gallstone size and the risk of gallbladder cancer. JAMA, 250: PP 2323-2326.
4. Tadashi Terada. Histopathological features and frequency of gallbladder lesions in consecutive 540 cholecystectomies Int J Clin Exp Pathol 2013;6(1):91-96.
5. Mohan H, Punia RP S, Dhawan SB, Ahal S and Sekhon MS. Morphological spectrum of gallstone disease in 1100 cholecystectomies in North India Indian journal of surgery vol.67, Num.3, 2005, PP.140-142.
6. Lazcano –Ponce EC, Miquel JF, Munoz N, Herrero R, Ferrecio C, Wistuba II et al (2001): Epidemiology and molecular pathology of gallbladder cancer. CA Cancer J. Clin, 51; PP 349.
7. S Singh, Ansari MA, Narayan G. Pathobiology of gall bladder cancer. Journal of Scientific Research, Banaras Hindu University, Varanasi Vol 56, 2012:35 ISSN: 0447-9483.
8. Jessuran J and Albores-Saavedra J .Gallbladder and extrahepatic biliary ducts, in Andersons Pathology. Edited by Damjanov I and Linder J, 10thEd Missouri, Mosby, 1996;vol 2: P 1859-1890.
9. Stirling GA. The gallbladder and extrahepatic bile ducts in Symmer's systemic pathology. Liver, Biliary tract and Exocrine Pancreas, 3rd Ed Edinburgh, Churchill Livingstone, 1994; vol 11: P 339-424.
10. Khan S, Jetley S and Husain M. Spectrum of histopathological lesions in cholecystectomy specimens: A study of 360 cases at a teaching hospital in South Delhi. Archives of international surgery/may-August 2013;Vol 3(2).
11. Stancu M, Caruntu I D, Giusca S and Dobrescu G. Hyperplasia, metaplasia, dyaplasia and neoplasia lesions in chronic cholecystitis- a morphologic study Romanian Journal of Morphology and Embryology 2007,48(4):335-342.
12. Shrestha R, Tiwari M, Ranabhat S K, Aryal G, Rauniyar S K and Shrestha H G. Incidental gallbladder carcinoma: value of routine histological examination of cholecystectomy specimens. Nepal Med Coll J 2010;12(2):90-94.
13. Hamilton SR and Aaltonen LA(Eds): World Health Organisation classification of Tumors. Pathology and Genetics of the digestive system IARC press: Lyon 2000.
14. Dursun N, Escalona OT, Roa JC, Basturk O, Bagci P, Cakir A et al. Mucinous Carcinomas of the Gallbladder Clinicopathologic Analysis of 15 Cases Identified in 606 Carcinomas. Arch Pathol Lab Med. 2012;136:1347–1358.
15. Mingoli A, Brachini G, Peteroni R, Antoniozzi A, Cavaliere F, Simonelli L et al. Squamous and adenosquamous cell carcinomas of the gallbladder. J Exp Clin Cancer Res. 24,1,2005.
16. Roa JC, Tapia O, Cakir A, Basturk O, Dursun N, Akdemir D et al. Squamous cell and adenosquamous carcinomas of the gallbladder: clinicopathological analysia of 34 cases identified in 606 carcinomas. Modern Pathology(2011) 24,1069-1078.