Histopathological spectrum of cholecystectomy specimens in a tertiary care hospital in Bangalore

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Abstract

Introduction: Gallstone disease is a major health problem and puts notable burden on individuals and health care system worldwide. This research was carried out to study the varied histopathological changes in the gallbladder mucosa as a result of cholelithiasis.

Materials and Methods: The present research comprised 190 gallbladder specimens obtained from cholecystectomy procedures conducted at tertiary teaching hospital in Bangalore. The gross examination was done after fixing the specimens with 10% formalin. Haematoxylin and eosin was used to stain gallbladder sections from fundus, body and neck.

Results: On gross examination, congestion was noticed on surface of gall bladder in 67 cases (35.26%), wall was thickened in more than half of cases 104 (54.74%). Nearly a quarter of specimens showed pathological changes in mucosa of gallbladder (23.15%). Histopathological examination observed evident epithelial hyperplasia in 80 cases (42.1%), antral metaplasia in 20 (10.5%), intestinal metaplasia in 12 (6.3%), dysplasia with carcinoma in one case (0.53%).

Conclusion: Gallstones produce a wide range of histopathological changes in mucosa and calls for dedicated attention of pathologist routinely.

Keywords: Cholelithiasis, Dysplasia, Hyperplasia, Metaplasia.

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Introduction

Gallstone disease is a fairly common condition at global level and constitutes more than 90% of biliary tract disease.[1] Gallstones are known to cause significant morbidity and mortality in all parts of the world.[2] Due to changes in dietary pattern with high calorie and high fat diet, and increased alcohol consumption the incidence of cholecystitis and cholelithiasis has shown an upward trend in the recent 3 to 4 decades[3,4] Gallstones prevalence is shown to vary with socio-demographic factors like age, sex and ethnic group. Majority remains unaware of the condition and lead asymptomatic course.[2]

Cholelithiasis is believed to cause varied histopathological changes in gall bladder mucosa like acute and chronic Inflammation, cholesterolosis, hyperplasia, metaplasia, dysplasia, and carcinoma.[5,6] The objective of the present study was to evaluate the histopathological patterns of gall bladder diseases and their incidences in patients undergoing cholecystectomy for cholelithiasis.

Materials and Methods

This prospective study was based on 190 gallbladder specimens obtained from cholecystectomy procedures conducted at a tertiary teaching hospital in Bangalore, during 2 years period from March 2015 to February 2017. This study was conducted at Dr. B R Ambedkar medical college, Bangalore. The gross examination was done after fixing the specimens with 10% formalin. Gross morphological findings of size, external surface, thickness of wall and mucosa were noted. For each specimen, three sections were obtained for entire thickness of wall from fundus, body and neck of specimen. Supplementary sections were taken from abnormal appearing foci. Routine tissue processing was done. 4 micron thickness sections were obtained from paraffin embedded tissue followed by routine Haematoxylin & Eosin staining and detailed microscopic evaluation. The data were entered and analyzed in MS Excel 2010 software and results presented in absolute numbers and percentages.

On microscopy, mucosa was examined for inflammation, cholesterolosis, hyperplasia, antral metaplasia, intestinal metaplasia, dysplasia and

carcinoma. Presence of inflammation (acute/chronic/granulomatous/eosinophilic/xanthogranulomatous), muscle hypertrophy and fibrosis in gall bladder wall was noted.

The following microscopic diagnostic criteria were used:

Cholesterolosis: Aggregates of cholesterol laden foamy macrophages.

Hyperplasia: Preudostratified epithelium, nuclear crowding, tall columnar cells.

Intestinal metaplasia: Presence of goblet cells.

Antral metaplasia: Mucous glands in lamina propria.

Dysplasia: Preudostratified epithelium, loss of polarity, nuclear crowding, nuclear atypia.

Carcinoma in situ: marked architectural atypia, full thickness marked nuclear atypia, atypical mitotic figures, absence of stromal invasion.

Carcinoma: Malignant glandular epithelium infiltrating into muscle layer along with desmoplastic change.

Results

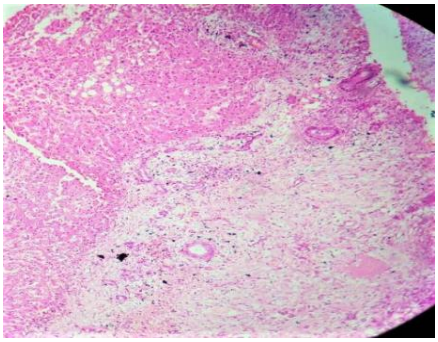

Fig. 1: Luschka ducts related to adjacent hepatic tissue

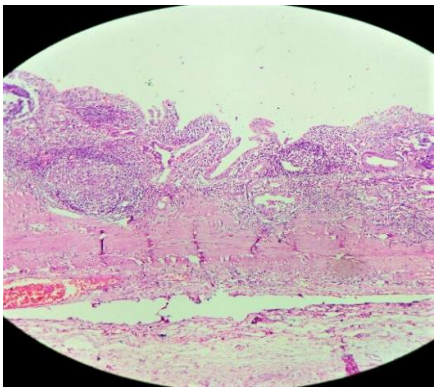

Fig. 2: Follicular cholecystitis

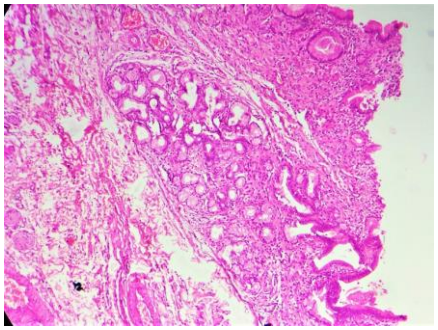

Fig. 3: Metaplastic change in mucosal epithelium

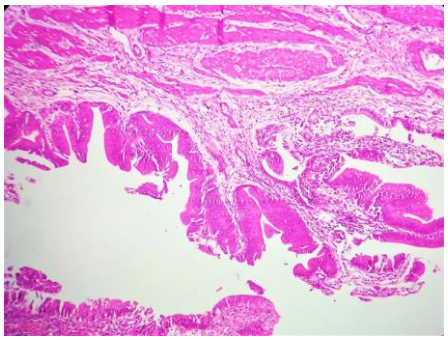

Fig. 4: Dysplasia in mucosal epithelium

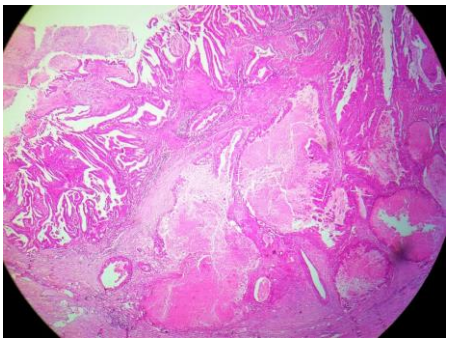

Fig. 5: Gallbladder Adenocarcinoma grade I

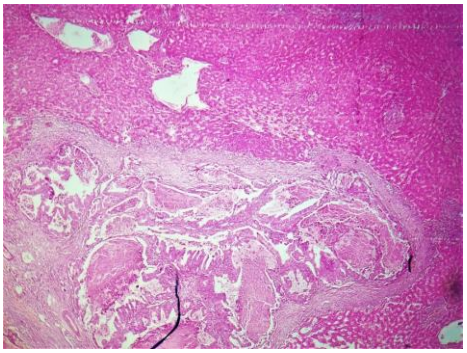

Fig. 6: Gallbladder Adenocarcinoma metastasized to Liver

A total of 190 cholecystectomy specimens were studied in two years duration. Female cases were twice the male cases (M:F ratio of 1:2.06). Age range of cases in the study was 21 to 82 years. Mean age was 43 years. Table-1 shows

age and sex distribution of cases. Over half of the cases occurred in 4th and 5th decades of life.

Gall bladder size was normal in 118 (62%), enlarged in 44 (23%) and fibrotic in 28 (15%) specimens. Table 2 shows the gross finding in gall bladder specimens. Surface of serosa was normal in 123 (64.74%) and congestion was evident in 67 cases (35.26%). Gallbladder wall was more than 3mm in thickness (thickened) in more than half of specimens 104 (54.74%). Mucosa appeared normal in majority of cases (76.84%). The number of gall stones and chemical composition of stones did not reflect much on gross changes.

In Specimens with mixed histopathological features, the categorization into one diagnosis per case was based on major changes observed. Normal epithelium was seen in 33 (17.3%), epithelial hyperplasia in 80 (42.1%), antral metaplasia in 20 (10.5%), intestinal metaplasia in 12 (6.3%), coexisting dysplasia was seen in one case of carcinoma (0.5%), and ulceration and fibrosis in 43 cases (23%).

Table 1: Age and sex distribution of cases (N=190)

Characteristic		No of cases	Percentage (%)
Gender	Male	62	32.63
	Female	128	67.37
Age group (in years)	21-30	26	13.68
	31-40	46	24.21
	41- 50	52	27.37
	51-60	40	21.05
	61-70	22	11.58
	>70	4	2.11

Table 2: Gross findings of Gall bladder specimens (N=190)

Gross finding	No of cases	Percentage (%)
Serosa		
Normal	123	64.74%
Congested	67	35.26%
Wall		
Normal	86	45.26%
Thickened	104	54.74%
Mucosa		
Normal	146	76.84%
Hemorrhagic	18	9.47%
Strawberry	26	13.68%

Table 3 shows distribution of cases by histopathological diagnosis. Commonest diagnosis was chronic cholecystitis (47.37%), followed by chronic cholecystitis with hyperplasia (21.05%) and metaplasia (16.84%).

One chronic cholecystitis case showed small tubular formations in the subserosal layer, on the hepatic side- Luschka ducts. These tubular structures are similar to Rokitansky-Aschoff sinuses, however, did not have any communication with them.

There was one case of well-differentiated conventional adenocarcinoma of gall bladder grade-1 in a 45 year old female. Dysplastic changes were present in the mucosa adjacent to the malignant foci. There was no lymphovascular and perineural invasion noted. However, metastatic deposits were noted in liver.

Table 3: Distribution of cases by histopathological diagnosis. (N=190)

Histopathological diagnosis	Number of cases	Percentage (%)
Acute cholecystitis	2	1.05
Chronic cholecystitis	90	47.37
Acute on chronic cholecystitis	6	3.16
Follicular cholecystitis	3	1.58
Chronic cholecystitis with hyperplasia	40	21.05

Chronic cholecystitis with metaplasia	32	16.84
Chronic cholecystitis with cholesterolosis	16	8.42
Adenocarcinoma of gallbladder	1	0.53

Discussion

Around 10-20% incidence range has been attributed to cholelithiasis at global level.[7] A further wider range of incidence has been reported for Indian population (2-29%).[2] Female preponderance to gall stone disease was very clearly noted in our study, similar to the finding in several other studies. Few studies reported this ratio to be as high as four times to six times.[8-10] inactive lifestyle and sex hormones have been incriminated in explaining the higher incidence of cholelithiasis for women in India.[2] Maximum incidence was noted in 4th and 5th decades in our study and the mean age was 43 years. This is comparable to age and gall stone findings observed in few other studies.[8-9,11] 41-50 years of life (5th decade) is reported to witness peak incidence.[10] In our study we did not get any case that was younger than 20 years of age during the study period. Several repeated occurrences of acute cholecystitis is thought to lead to chronic cholecystitis and gallstones are thought to be the main triggering condition for this.[12]

Epithelial hyperplasia was the most common finding in the present study (42.1%), followed by metaplasia (16.8%). This finding is similar to the observation in other studies.[9,11] A small percentage of hyperplasias are believed to advance towards atypical hyperplasia, which further most likely progresses to carcinoma in situ and carcinoma.[13] It is proposed that, gallstones, by way of causing mechanical irritation, progress primary cholelithiasis to secondary hyperplasia.[14] Metaplasia was the second most common change seen in our study (16.8%) and antral metaplasia being more common than intestinal metaplasia. A similar incidence of 16% was noted in khanna et al and mathur et al studies.[9-10] However, frequency of metaplasia can be seen in more than half of the cases with gallstone disease as reported in few other studies.[15-16] Metastatic epithelium is considered to be more prone to malignant transformation than normal epithelium.[17] Normal epithelium and metastatic epithelium could be two pathways by which gallbladder cancer can result.[17]

Epithelial dysplasia was found in one case of carcinoma in the present study (0.53%). Few other researchers noted dysplasia in 1.3% and 2.2% of cases in their studies.[11,17] However, one study reported dysplasia at 8.5%.[9] Discrepancy may be due to number of specimens in each study, and number of sections examined and also the severity of gall bladder cases presenting to different clinical settings.

On macroscopic examination, many in situ carcinomas are overlooked or missed, due to the fact that these are not clearly differentiable from cholecystitis on gross examination. The gall bladder wall thickness and mucosa may show mild changes or remain normal on gross. This poses difficulty for a pathologist who may have no standard guide as to where to take the representative section. This could be the reason for underestimation of the incidence of in situ carcinoma.[9]

Chronic cholecystitis with cholesterolosis was noted in 8.5% in the present study. Cholesterolosis was found in 13% to 14% cholelithiasis specimens in two other studies.[11,18] There was no case of carcinoma in situ in the present study but one case of carcinoma was observed (0.53%). A similar percentage of gall bladder carcinoma was noted in asymptomatic cases in another study (0.57%). Studies have shown that incidental gallbladder carcinoma is found in about 0.5-1.1% of cholecystectomies for gall stone diseases.[19-20] The incidence of gallbladder cancer is reported to be higher in certain geographic areas, like the Karachi to Kolkata belt in the Indian subcontinent.[21-22] Reasons for different incidences in different studies could be due to geographical region, severity of cases presenting to different settings, number of sections taken to examine for each specimen and deviation from uniform criteria for classifying microscopic findings.

Conclusion

Gallstones present with varied histopathological changes ranging from inflammation to malignancy. Chronic cholecystitis is the commonest histopathological finding in in gall stone diseases. Hence, we recommend detailed histopathological evaluation of all cholecystectomy specimens for timely diagnosis and prompt intervention.

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