

Importance of Histopathology in Routine Cholecystectomies

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Abstract

Introduction: Gall bladder is one of the common histopathological specimen received in pathology department during routine practice. Many a times premalignant changes, in-situ and invasive carcinomas are found as incidental findings in histopathology (HPE).

Objectives: To know the incidence of various histopathological lesions which are most of the times incidentally identified in routine and elective cholecystectomies at our institution.

Materials and Method: The study was conducted from January 2016 to June 2016. The gross specimen of gall bladder was received for histopathological examination at department of pathology. Gross examination findings of the specimen were recorded. If any calculi were present, their type and number were documented. Eight bits were sampled with 4 bits in one capsule.

Results: 107 gall bladder specimens were received during the study period. A female preponderance was seen in our study with male to female ratio of 1:2.2. Majority of the cases seen were between 31-40 yrs. 97.3% cases were non neoplastic lesion and 2.7% were neoplastic. 18 cases had metaplasia, out of which 13 cases (12.1%) showed antral type metaplasia, 2 cases (1.9%) of intestinal metaplasia and 3 cases (2.8%) with both antral and intestinal type metaplasia was seen. One case of biliary intra epithelial neoplasia grade II (0.9%), one case of biliary adenoma (0.9%) and one case of invasive adenocarcinoma of gall bladder (0.9%) were incidentally identified.

Conclusion: Although most of the cholecystectomies are elective done for cholecystitis a varied histopathological types of the lesions can be seen in gall bladder. Thus a meticulous and detailed examination of both gross and microscopy by sampling more bits is essential. Hence routine histopathological examination is gold standard and is mandatory for all cholecystectomy specimens.

Keywords: Cholecystitis, Metaplasia, Carcinoma, Routine HPE.

Introduction

Gall bladder is one of the common histopathological specimens received in pathology department during routine practice.⁽¹⁾ Although most of the cholecystectomies are elective and done for pain abdomen with ultrasound features of cholecystitis with or without calculi, a diverse histomorphological spectrum of lesions can be seen in the gall bladder during routine histopathological examination. Often premalignant changes, carcinoma in-situ and invasive carcinomas are found as incidental findings in histopathology. The commonest hepatobiliary malignancy is gall bladder carcinoma. Advanced malignancy will have poor prognosis. Routine HPE will help in detecting early malignancies.

Objectives

We studied all the cholecystectomy specimens at the Department of Pathology, Bangalore Medical College and Research Institute from January 2016 to June 2016, to know the incidence of various gall bladder lesions at our institute. To detect the incidence of early malignant and premalignant lesions. To evaluate the utility of routine HPE of cholecystectomy specimens.

Materials and Methods

Specimens of gall bladder were received for histopathological examination (HPE) at the Department of Pathology along with the requisition containing

clinical details of the patient. Informed consent was taken from the patients for the study. 10% formalin was used as the preservative. The clinical details of the patients were noted. Gross examination findings of the specimen were recorded. If any calculi were present, their type and number were documented. Eight bits were sampled with 4 bits in one capsule. The bits were subjected to regular histokinete processing and H&E (Hematoxylin and Eosin) staining. The slides received were then studied and the microscopic findings were noted.

Results

107 gall bladder specimens were received during the study period and were included in the study. Out of these, 74 specimens were from females and 33 were from males. A female preponderance was seen in our study with male to female ratio of 1:2.2. The age of presentation ranged from 3 yrs. to 70 yrs. with majority of the cases seen between 31-40 yrs. The age wise distribution the cases are as shown in Fig. 1. In two cases, cholecystectomy was done in 3yr and 5yrs. old children, with choledochal cyst. The gall bladder in both these cases showed mild, chronic inflammatory changes. Although most of the cases were received with the clinical diagnosis of cholecystitis, various types of lesions were found on histopathological examination as in Table 1. Out of 107 cases studied, 104 cases (97.3%) were non neoplastic lesions and 2.7% were neoplastic

lesions. One case of biliary intra epithelial neoplasia grade II (0.9%), one case of biliary adenoma (0.9%) and one case of invasive adenocarcinoma of gall bladder (0.9%) were seen in our study as in Fig. 2. Chronic cholecystitis was the commonest lesion found in our study with 67 cases out of them having calculi. 23 cases were non calculus chronic cholecystitis. 18 cases had metaplasia, out of which 13 cases (12.1%) showed antral type metaplasia, 2 cases (1.9%) of intestinal metaplasia and 3 cases (2.8%) with both antral and intestinal type metaplasia were seen. Both intestinal and gastric metaplasia has been shown in Fig.3. The xanthomatous change is shown in Fig.4.

Table 1: Table showing distribution of various pathological lesions in cholecystectomy cases

Diagnosis	No. of cases	Percentage
Chronic cholecystitis	90	84.1%
Acute cholecystitis	3	2.8%
Acute on chronic cholecystitis	6	5.6%
Granulomatous cholecystitis	1	0.9%
Xanthomatous cholecystitis	2	1.8%
Sclerosing cholecystitis	1	0.9%
Lymphoplasmacytic cholecystitis	1	0.9%
Biliary adenoma	1	0.9%
Gall bladder adenocarcinoma	1	0.9%
Biliary intra epithelial neoplasia	1	0.9%
Total	107	

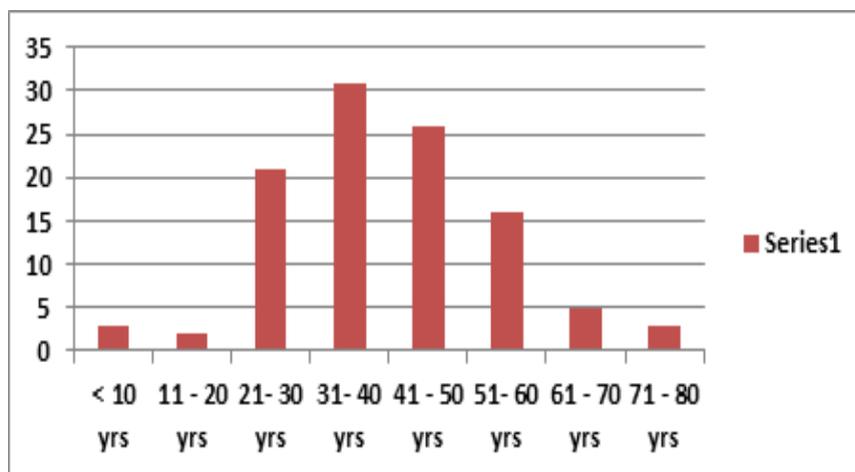


Fig. 1: Age wise distribution of cholecystectomies

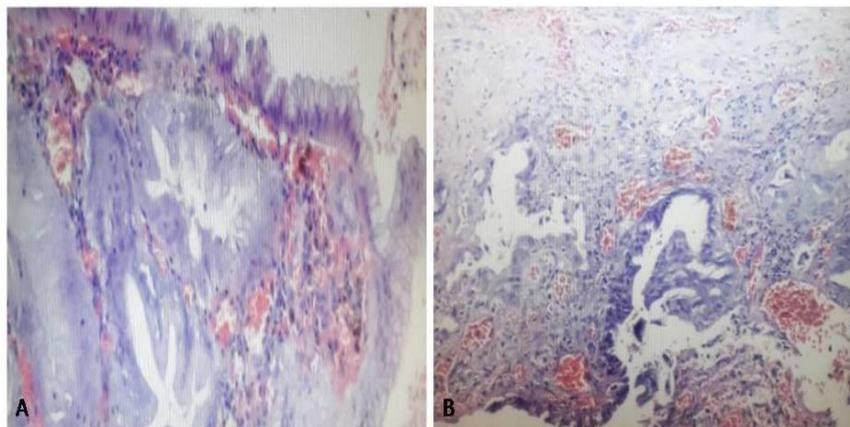


Fig. 2. Showing features of gall bladder malignancy

Legends: A showing surface epithelium of gall bladder showing intestinal metaplasia and underlying tumor with glandular pattern. B showing infiltration of muscularis layer by the tumor cells.

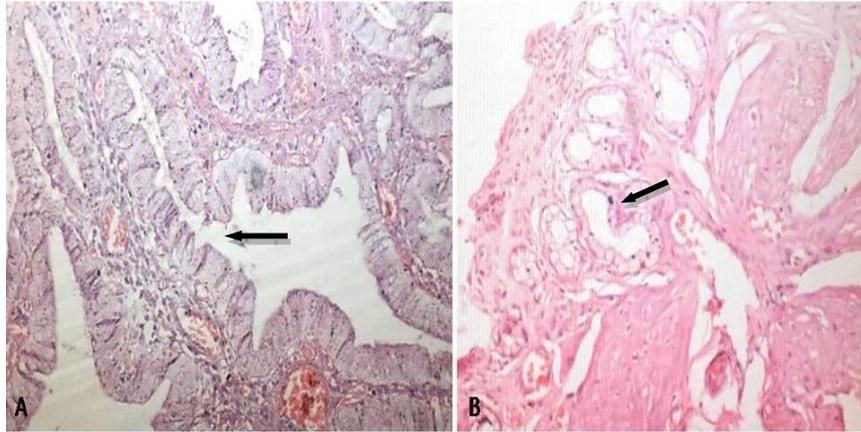


Fig. 3: Showing intestinal and gastric metaplasia

Legends: A showing intestinal metaplasia of the epithelium with arrow pointing goblet cells. B shows antral metaplasia with arrow pointing pseudoantral glands.

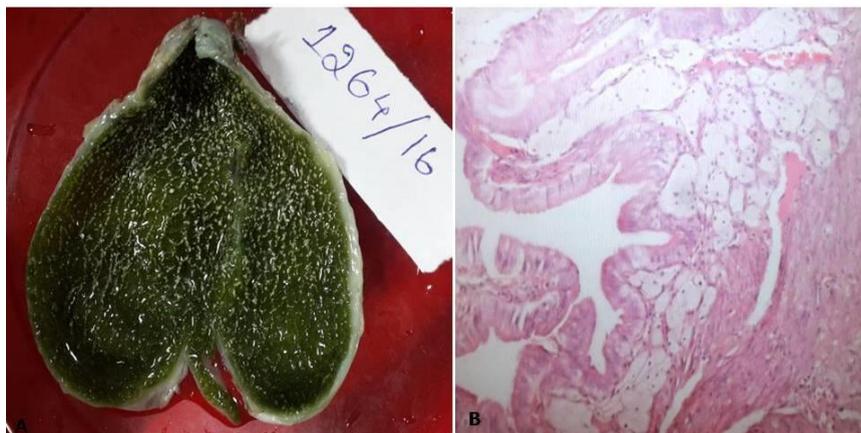


Fig. 4: Showing gross and microscopy of Xanthomatous change in chronic cholecystitis.

Legends: A shows velvety mucosa with multiple grey white chalky papules. B showing sheets of foamy macrophages in lamina propria with mucosa showing intestinal metaplasia.

Discussion

Gall bladder is one of the common surgical specimens received for histopathological examination. A female preponderance in gall bladder lesions is observed as seen in many studies and our study.^(1,2) Presence of calculi with evidence of chronic cholecystitis is the commonest finding on histopathological examination. The calculi are of both pigment type and cholesterol type.

Patients of gallstones are prone for carcinoma with a relative risk of 4.9.⁽³⁾ Chronic irritation of the mucosal surface of the gall bladder due to chronic inflammation and cholelithiasis results in metaplasia. Many studies have shown that pseudo gastric type of mucosal metaplasia is seen in younger age while intestinal type of metaplasia is seen in higher age group patients. Also, the prevalence of metaplasias has been variable in different studies, ranging from 9% to 73%.⁽⁴⁾ Metaplasia was seen in 16.8% cases in our study. Many studies have

suggested that antral type metaplasia and intestinal type metaplasia are precursor lesions of gall bladder dysplasia and carcinoma.⁽⁵⁾ Several studies have reported metaplasia in younger age group, and have demonstrated an age gradient from metaplasia to dysplasia.^(6,7) In our study, majority of the metaplasias were seen in patients < 50 years of age, and in 4 cases metaplasia was seen in patients more than 60 years of age. The gall bladder malignancies associated with metaplasia have been described to be more common and associated with better prognosis than malignancies without any metaplasia.

In our study one case of biliary type gall bladder adenoma (0.9%) was incidentally identified. It is one of the rare lesions incidentally found in gall bladder presenting with cholelithiasis with the documented incidence being 0.3% - 0.5%.^(8,9) One case of invasive gall bladder adenocarcinoma – pancreatico-biliary type was identified during the study period which clinically presented as acute cholecystitis with perforation. Gall

bladder malignancy has a poor prognosis and early detection of the lesion is of survival benefit.

Gallbladder cancer is the most common malignancy of the extrahepatic biliary tree worldwide.⁽¹⁰⁾ It is more common in the seventh decade of life. Women are at higher risk than men in developing this disease.⁽¹¹⁾ Diagnosis is often made in the advanced stage with a poor prognosis; an overall mean survival of six months and a five year survival rate of less than 5%.⁽¹²⁾

Early-stage tumours are associated with good prognosis. Their clinical presentation may be non-specific with symptoms similar to those of acute or chronic cholecystitis. In our study Gall bladder cancer (GBC) and other premalignant lesions were identified for the first time on histopathological examination. GBC that is detected for the first time on histopathological examination in a gallbladder removed for other gallstone disease is called Incidental Gall Bladder Carcinoma (IGBC). The incidence of IGBC has been reported to be 0.3–1.5% in various case series.⁽¹³⁾ The overall prognosis of GBC is poor, but IGBC is associated with a better prognosis.⁽¹⁴⁾ Early-stage tumours for which surgical resection provides the greatest benefit are difficult to diagnose preoperatively. These are usually missed even after intraoperative examination of the cholecystectomy specimen.^(10,12) Detection of GBC on histopathology allows early detection of malignancy, their follow up and complete radical cholecystectomy which remains the treatment of choice for IGBC of stage Ib and beyond.⁽¹⁴⁾

Histopathological examination of cholecystectomy specimens allows the detection of tumours that are not apparent even on gross examination of the specimen.⁽¹⁰⁾ Hence the standard practice has been to submit all gallbladders removed for presumed gall stone disease (GSD) to routine HPE to exclude gallbladder malignancy.⁽¹⁵⁾

Whether routine histopathology of all cholecystectomy specimens should be done or not is a matter of debate. Rarity of incidental gallbladder carcinoma along with high load of cholecystectomy specimens demands a selective approach for histopathological analysis to improve its cost effectiveness. On the other hand, aggressive nature of tumor along with unfortunate diagnostic misses in early stage demands routine analysis especially in high risk zones of gallbladder carcinoma.⁽¹⁶⁾

Recently, however, various reports in the literature have questioned the role of routine HPE in all cholecystectomy specimens.⁽¹⁷⁻²¹⁾ The various reasons given are: (1) the incidence of IGBC is too low to justify routine HPE of all cholecystectomy specimens, (2) routine HPE of all cholecystectomy specimens overburdens pathology and hospital resources, (3) almost all cases of IGBC are associated with positive findings on gross examination of the gallbladder when it is cutopened and examined on Table, (4) simple cholecystectomy is adequate for early-stage tumors which include carcinomas in situ and T-stage Ia tumors.

Some reports support the claim that the examination of the cholecystectomy specimens in the operating room reveals some suspicious findings in all cases of IGBC. Darmas et al reported IGBC in only four of 1452 (0.3%) patients for whom cholecystectomy specimens were examined over a period of 5 years. All four cases demonstrated a mass on gross examination of the cholecystectomy specimen and two of whom showed preoperative suspicion of malignancy.⁽²⁰⁾ Bazoua et al.⁽¹⁸⁾ reported an analysis of 2890 cholecystectomy specimens, in which malignancy was seen in 10 cases, all of which had demonstrated thick-walled gallbladders on gross examination and in two of which suspicious mass had been apparent.

However, several authors have reported that preoperative imaging findings and intraoperative gross examination may not be reliable in identifying malignancy.^(10,22) Roa et al., observed that 37% of primary tumours were macroscopically in apparent.⁽¹¹⁾ In a retrospective analysis of 503 cholecystectomy specimens conducted by Anil K. et al,⁽²²⁾ reported that 33 patients had shown intraoperative suspicion for malignancy where the gallbladder was sent for frozen-section examination. Of these, only five patients had evidence of malignancy. Of the remaining 470 specimens in which there was no suspicion of malignancy on macroscopic examination, GBC was diagnosed in four cases. Thus, it is evident that, despite careful macroscopic examination, GBC can be missed and that implementing a policy of selective HPE of cholecystectomy specimens will fail to identify tumours in patients who might otherwise have a good prognosis.⁽²²⁾

In patients with GBC, a radical resection is the only hope for cure. In India, it is a common practice that cholecystectomy specimens are not sent for HPE, especially in peripheral centres. As a result, many patients present late at a time when their disease is usually advanced or metastatic. Based on this analysis, it is recommended that all cholecystectomy specimens should be opened and examined. Cases where findings on intraoperative examination are suspicious should be sent for frozen-section examination of the cholecystectomy specimen. In all other patients, the cholecystectomy specimen should be sent for routine HPE so that the detection of early GBC is not missed in a subgroup of patients who might derive maximum benefit from radical resection.⁽²²⁾

Conclusion

Although most of the cholecystectomies are elective and done for cholecystitis, varied histopathological lesions can be seen in the gall bladder. As most of the lesions are incidentally identified, we conclude that all gall bladder specimens should be subjected to routine HPE. A meticulous and detailed examination of both gross and microscopy by sampling more bits is essential. More number of bits should be submitted for microscopy

as compared to conventional three bits. However, more studies on identifying ideal number of bits required for diagnosis of unsuspected lesions without over burdening the histopathological load is essential.

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