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Original Research Article

Surgeons Throw Pathologist Catch – A Spectrum of Histomorphological Patterns in Gall Bladder Lesions

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Abstract:

Background: Gall bladder lesions are remaining exceedingly ubiquitous and often needs surgical intervention. The histopathological patterns represent a spectrum, ranging from cholecystitis to gallbladder carcinoma. Histopathological analysis provide definitive diagnosis on resected specimen and hence ultimately help in further future management. Amongst all lesions cholecystitis with Cholelithiasis is known to produce diverse histopathological changes in the gallbladder mucosa .The present study aims to define the occurrence of various gallbladder lesions on histology.

Method: This was a prospective observational study conducted in the Department of Pathology at Teaching Institute in Central India. The study period was two year, from first January 2021 to 31st December 2022. A total of 185 patients who underwent cholecystectomy at the institute were included in the study. Gross features of cholecystectomy specimens were recorded. Three sections each from the neck, body, and fundus were taken. Histopathological diagnosis was correlated with demographic data.

Results: Total 185 patients were included, out of which 130 were females and 55 were males, with the mean age 45 years. 180 cases associated with different types of gall stones. The most common histopathological findings were chronic cholecystitis, observed in 164 patients i.e. 88.64% followed by adenocarcinoma of gall bladder 9 patients, 7 patients with acute cholecystitis, 3 patients having xanthogranulomatous cholecystitis.

Conclusion: Diseases of the gallbladder often mandate prompt surgical intervention. Chronic cholecystitis, which is an established risk factor for gallbladder carcinoma, is one of the commonest presentations. Therefore detailed and meticulous histopathological examination remains crucial in the detection of premalignant and malignant lesions.

Keywords: Gall Bladder, Cholelithiasis, Histomorphology.

Introduction

Chronic cholecystitis and cholelithiasis is a very common health problem, all over the world affecting around 10% to 15% of the adult population living in developed countries and most prone for surgical procedure. [1,2,3,4] Cholelithiasis is the most common risk factor for gall bladder carcinoma (GBC) amongst various factors. [2,5]. Hence Gall bladder is most commonly received specimens in any histopathology laboratory. [6,7]

A broad gamut of diseases, occur in the gall bladder. They range from congenital anomalies, non-inflammatory, inflammatory diseases, calculi and its complications, and neoplastic lesions. The gall bladder lesions are classified into non-neoplastic and neoplastic diseases.[8,9] Cholecystitis can be clinically diagnosed by the history, physical examination, laboratory and radiological investigations. Histopathology is the gold standard for the diagnosis of cholecystitis. Calculi cause various histomorphological changes in gall bladder mucosa which includes different types of metaplasia, glandular hyperplasia, xanthogranulomatous cholecystitis, cholesterosis and malignancy. [10]

GBC is rare condition with a poor prognosis. The incidence of gall bladder carcinoma (GBC) is 0.8-1%. Cholelithiasis is found in approximately 85%

of people with GBC.8 Gall bladder carcinoma (GBC) arises from the abnormal proliferation of the epithelial lining of gall bladder and cystic duct. [8,10,11,12] The prevalence of gall stone diseases shows a marked geographic and ethnic variation. [2,13] Percentage of prevalence of gall stone in Asian population is 3-5%, many of them are symptomatic.[4] Central India along with the North, East, and Northeast areas of India has a high incidence of gallbladder cancer, in contrast to South and West India.[3]

This study was performed in one of the teaching institute of Central India, to examine the various histomorphology of cholecystectomy specimen received in the Pathology department of our institute.

Material and Methods

This was a prospective observational study conducted in the Department of Pathology at a teaching Institute in Central India. The study period was two year, from first January 2020 to 31st December 2021. A total of 185 patients who underwent cholecystectomy at the institute were included in the study.

Inclusion criteria: All cholecystectomy specimens received in the Department of Pathology during the study period were included in the study.

Exclusion criteria: Gall bladder excised with duodenum and pancreas (Whipple procedure) was excluded.

Cholecystectomy specimens were fixed in 10% formalin. Gross features of specimens were recorded. Three sections each from the neck, body, and fundus were taken. Additional sections were taken from pathological areas like growth, irregularity and thickening in the wall, calcification, and necrosis following standard grossing techniques. Routine tissue processing and staining was performed. A proper histopathological examination of the slides was done.

Patient's demographic data, type of operation performed, relevant investigations, radiological findings and histopathological diagnosis were collected in a database for further analysis.

Results

A total of 185 patients who had undergone cholecystectomy were studied. These included 130 (70.27%) females and 55 (29.72%) males. The male to female ratio was 1:2.36. The youngest patient was a 15 years old female and the eldest patient was a 74 years female. The maximum number of patients i.e, 48 patients (25.94%), were in the age group of 31 to 40 years, followed by 38 patients (21.81%) in the age group of 41-50 years, The mean age was 45 years.

Out of the total 185 cases, laparoscopic cholecystectomy was done in 160 cases. 23 cases had open cholecystectomy and two cases had open cholecystectomy with extended hepatectomy. Open cholecystectomy with extended hepatectomy was done in two patients with pre-operative diagnosis of gall bladder carcinoma (GBC). Out of 185 cases, 176 were Non-neoplastic and 9 were malignant cases. Gall stones were present in 180 cases (97.29%).(Fig.1)

All the three cases of adenocarcinoma were associated with gall bladder stones. Most common gall stones were pigmented stones seen in 163 cases. These pigmented stones were multiple, subcentimetric and dark green to black in colour. Pigment stones were found to be most common followed by cholesterol stones. Cholesterol stones were present in 17 cases and these stones, were yellowish white in colour, larger then pigmented stones, one to two in number and ranging in size from one to three centimetres in greatest dimension.

Clinical presentation: The most common clinical presentation was chronic pain in abdomen in 168 cases (90.81%). These patients complained of pain in epigastrium. 34 (18.37 %) patients also had nausea, vomiting. 13 (7.02%) patients, had intolerance to fatty food.

Non neoplastic cases

162 cases were of chronic cholecystitis (Fig. 2) accounting for the maximum number of gall bladder diseases. Amongst its 160 were with cholelithiasis and two were of chronic acalculous cholecystitis.

The gross and microscopic picture of both chronic calculous cholecystitis and chronic acalculous cholecystitis was the same, except for the presence and absence of gall stones. On gross examination the gall bladder was normal to shrunken with unremarkable serosa. On microscopic examination, chronic inflammatory infiltrate in the mucosa, lamina propria was noted and Rokitansky Aschoff sinuses were seen in few cases.

Two cases of acute- on- chronic calculous cholecystitis showed thickened wall with ulcerated and haemorrhagic mucosa. On microscopy there were large areas of oedema, haemorrhage, mixed inflammatory infiltrate in fibrotic wall.

Xanthogranulomatous cholecystitis (XGC)(fig.3) is a variant of chronic cholecystitis. The gallbladder shows focal or diffuse destructive inflammatory process, with proliferative fibrosis, along with infiltration of macrophages and foamy cells.14,15 There were 3 cases of xanthogranulomatous cholecystitis. On gross examination irregular thickening of gall bladder with yellow nodule were seen. On microscopy there was mucosal ulceration,

marked infiltration of lipid laden macrophages and fibrosis. One of the cases of xanthogranulomatous cholecystitis in addition showed, intestinal metaplasia. There were 9 cases of GBC. 6 cases were diagnosed preoperative on CT scan. 3 cases were incidentally diagnosed on histopathology. One case was clinically suspected as malignancy and was confirmed on histopathology.

All the cases were of 5th to 6th decade and 6 were female. On gross, gall bladder showed thickened wall with exophytic cauliflower like lesions. 3 cases which were diagnosed incidentally show thickened rough gall bladder mucosal surface with multiple calculi. So clinically and radiological diagnosed as calculus cholecystitis. On microscopic examination, glands lined by columnar cells with hyperchromatic nuclei and minimal desmoplasia were seen.

These malignant cells infiltrated the muscle coat and also showed vascular invasion Hence diagnosis provided was well differentiated adenocarcinoma of GB- pT1b.(Fig.4)

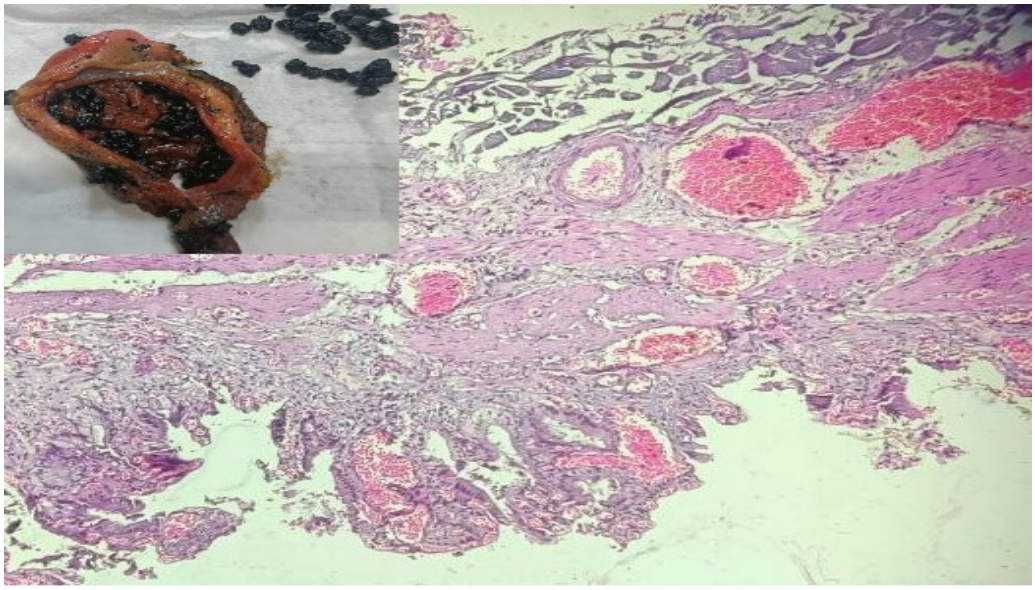

fig 1- Chronic cholecystitis (10X) lymphocytic infitrate with congestion , inset - multilple stones

Figure 1: Chronic cholecystitis (10X) lymphocytic infiltrate with congestion, inset-multiple stones

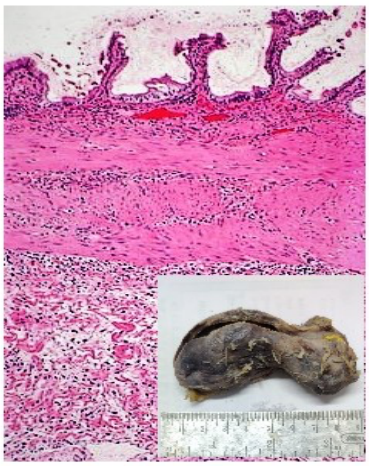

Fig 2 Acute cholecystitis (10X)

Figure 2: Acute cholecystitis

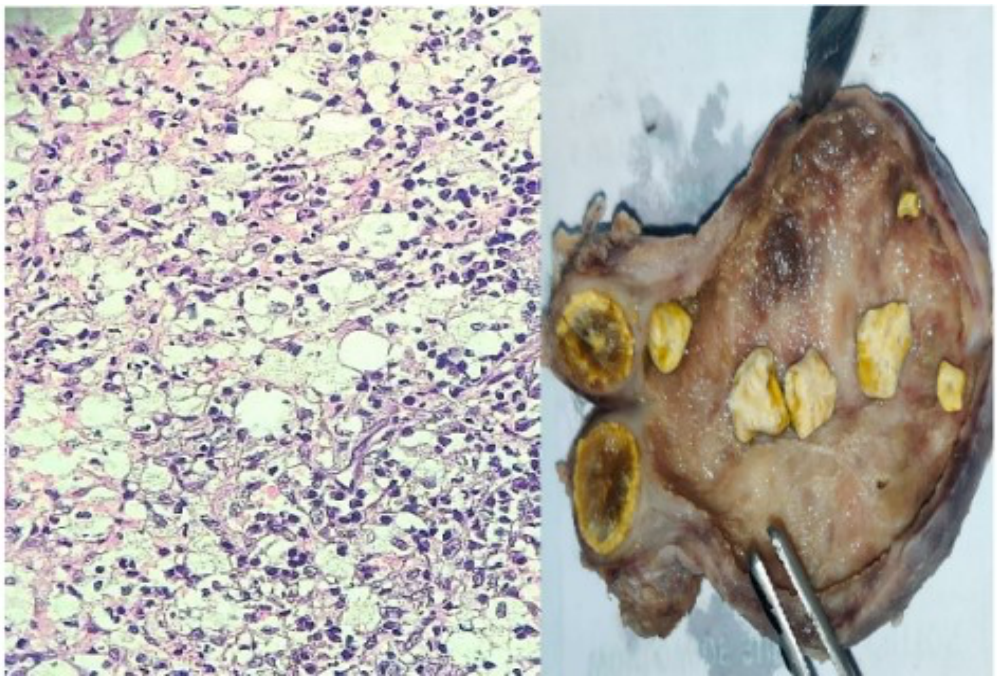

Figure 3: show transmural foamy histiocytes with lymphocytes (40X) Gross – thick wall gall bladder with multiple yellow stones

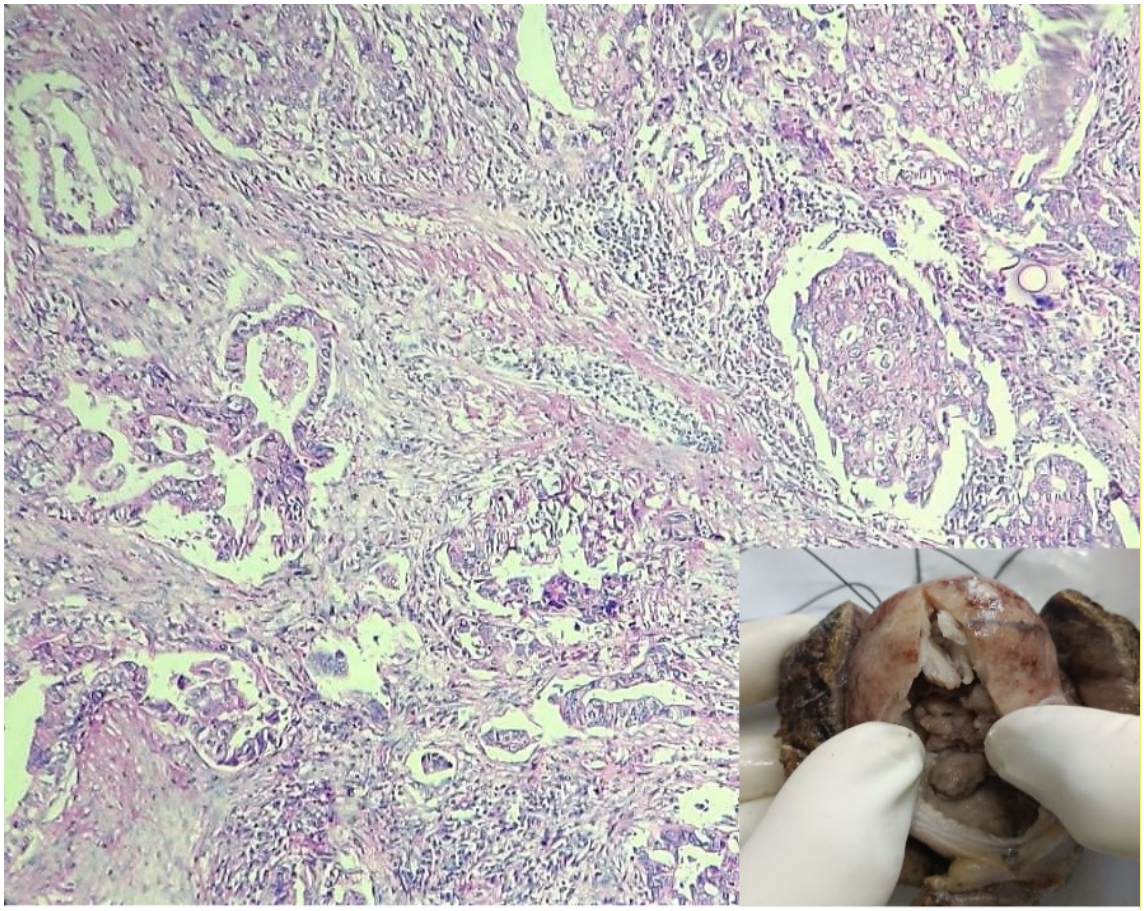

Figure 4: show malignant glands in muscle with desmoplasia (40X) Gross – exophytic mass in fundus

Discussion

In the present study, the female patients outnumbered the male patients with a male to female ration of 1:2.36 which is in concordance with other studies. [4,6,8] Female gender is noted to be a risk factor that predisposes to the development of gallstones. There is a rising trend

in the gall bladder disease. This is attributed to rapid urbanization, change in life style and dietary habits, and mainly increase in consumption of fat and low dietary fibre intake. [16] In our study, almost all the patient's i.e, 94.5% presented with cholelithiasis, which can eventually herald the onset of various pathologies, such as acute cholecystitis, chronic cholecystitis, follicular cholecystitis, cholesterolosis and malignancies. Chronic cholecystitis, the most common pathology was noted in 1624 patients i.e, 88.64 %. out of which 160 cases (97.56 %) was associated with calculi. [1,4,8,13,17] There was no significant difference noted in gross as well as histological features of chronic calculus cholecystitis and chronic acalculus cholecystitis. [1,4,8,13,17],

The incidence of xanthogranulomatous cholecystitis (XGC) ranges from 0.7 to 10%.14,15 In the present study there were two (3.6%) cases of XGC. Similar incidence was reported by Sabina Khan et al.17 XGC accounted for 1.24% by Talreja V et al, 1.2 % by Dincel O et al and 2.3% by Jokhi CD et al., [4,13,1] Involvement of Rokitansky-Aschoff sinuses and extravasation of bile into the gallbladder wall is a probable precipitating factor for XGC. The gall bladder wall is diffusely involved with thickness ranging from 4 mm to 18.5 mm.

Many studies reported cases of chronic follicular and chronic eosinophilic cholecystitis. [1,6,8] In the present study such entities were not seen. Cholesterolosis which is a benign condition results from accumulation of triglycerides and cholesterol esters in the macrophages within the gallbladder wall. It occurs in two forms localized and diffuses (strawberry gallbladder). Cholesterolosis was found in 1.27% of the specimens in some studies. [4,17] There was no case of cholesterolosis in the present study.

Metaplastic changes can occur in gall bladder and could be pyloric or intestinal. In the present study intestinal metaplasia was seen in one case with xanthogranulomatous cholecystitis and mild changes may be missed. Thorough sampling of the gallbladder specimens and meticulous interpretation is required to study metaplasia in gallbladder specimens. [16] There are unmodifiable and modifiable risk factors for the gall stone diseases. The unmodifiable conditions are, aging, female gender, races, and lithogenic (LITH) genes. There are a number of modifiable conditions. [3,16]

Gall stones- there are different types of gall stones the appearance of the stone differs with its cholesterol content.

GBC is the most frequent malignancy of the biliary tract. It is the fifth most common gastrointestinal malignancy. [4,13] The abnormal proliferation of the epithelial lining of the gallbladder (GB) and the cystic duct gives rise to gall bladder carcinoma (GBC), which is the most common biliary tract malignancy worldwide. GBC on gross shows, diffusely thickened GB wall or a mass arising from the fundus, neck, or body of the GB. In the early stage of GBC, the symptoms are similar to that of benign lesions like chronic cholecystitis or it can be asymptomatic. GBC has a high mortality rate and is rapidly progressive. Diagnosing GBC at an early stage is desirable as it favours good prognosis.

Age increases the incidence of GBC. Availability to the health care facility and increase public awareness has lead to the early detection of GBC. Early diagnosis of GBC is tough on clinical and radiological findings. Diffuse gall bladder wall thickening and intra luminal mass can be seen on radiology in GBC. After Ultrasonography, GBC is diagnosed in about 40-60% cases after the development of intra luminal mass.

Diffuse gall bladder wall thickening can be seen in both chronic cholecystitis and GBC. Which sometimes give false impression of benign lesion. Hence incidental gall bladder carcinoma always surprises surgeon and pathologist. In our study we found 3 cases of incidental gall bladder carcinoma i.e.1.8%. Other studies also noted the incidence 0.2-3.3%. [4,6,7,8,13,18] Pain in abdomen was the most common clinical presentation in 168 cases (90.81%) followed by nausea and vomiting in 34 patients (18.37%). This was in concordance with the other studies. [8,9,17,19]

Out of the total 185 cases Laparoscopic cholecystectomy was done in 160 cases. 23 cases had open cholecystectomy and two cases had open cholecystectomy with extended hepatectomy. Open cholecystectomy with extended hepatectomy was done in patients with pre-operative diagnosis of gall bladder carcinoma (GBC). This finding is similar to other studies. [1,8] The recommended gold standard treatment for symptomatic gall stone patients is laparoscopic cholecystectomy. [20]

Conclusion

Diseases of GB is always remains a major indication for cholecystectomy. Hence one can evaluate wide spectrum of histomorphological lesions on postoperative excised specimens.

Amongst various lesions we encountered, chronic cholecystitis, cholesterolosis, and acute-on-chronic cholecystitis remains the most prevalent. Furthermore, a macroscopic absence of remarkable features does not exclude the presence of an underlying premalignant or malignant lesion.

So routine histopathological examination of the resected GB specimens is mandatory in search of premalignant precursor such as intestinal metaplasia and reactive atypia. These lesions can

progress to GB adenocarcinoma, which is noted to have a particularly forbidding prognosis.

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