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RESEARCH ARTICLE

A STUDY ON MICRO ANATOMICAL CHANGES IN THE VARIOUS GALL BLADDER DISEASES

[1]Lt Col (Dr) Vds Jamwal, *,[2]Major(Dr) Mohan Angadi and [3]Col(Dr) Sushil Kumar

[1]Assistant Professor/ Clinical Embryologist, Department of Anatomy, Armed Forces Medical College (AFMC), Pune-411040
[2]Assistant Professor, Department of Anatomy, Armed Forces Medical College (AFMC), Pune-411040
[3]Professor and Head, Department of Anatomy, Armed Forces Medical College (AFMC), Pune-411040

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ABSTRACT

The gall bladder is a flask shaped, blind ending diverticulum which lies attached to the inferior surface of the right lobe of liver by connective tissue. It is attached to the common bile duct by the cystic duct. The gall bladder is about 7 to 10 cm long with a capacity of about 50 ml. It usually lies in a shallow fossa in the liver parenchyma covered by peritoneum which continues from inferior surface of liver. The primary function of gall bladder is to store and concentrate bile. This concentration is done by absorption of water and inorganic salts through the epithelium into the vessels of the lamina propria of its mucosa (1). Gall bladders are one of the more frequently encountered specimens in the surgical pathology laboratory. They are usually removed for stones and/or inflammatory conditions, but rarely may they harbor a neoplasm. Gall stones are a major cause of morbidity and mortality throughout the world. Cholecystectomy is the means by which the pathologist can diagnose the most common pathology of the gall bladder, which is chronic cholecystitis typically accompanied by cholelithiasis. By studying the histopathological changes the pathologist can diagnose chronic cholecystitis, which is typically accompanied by cholelithiasis. About 10% of the adults have gallstones(2,3).There is a female to male ratio of about 2 to 1 in the younger age groups, and with advancing age there is increasing prevalence in females. After the age of 60 yrs about 10 to 15 % of men and 20 to 40 % of women have gall stones (2). The risk of gall stones is also associated with a history of childbearing, estrogen replacement therapy, oral contraceptive use and marked obesity.

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INTRODUCTION

The gall bladder is a flask shaped, blind ending diverticulum which lies attached to the inferior surface of the right lobe of liver by connective tissue. It is attached to the common bile duct by the cystic duct. The gall bladder is about 7 to 10 cm long with a capacity of about 50 ml. It usually lies in a shallow fossa in the liver parenchyma covered by peritoneum which continues from inferior surface of liver. The primary function of gall bladder is to store and concentrate bile. This concentration is done by absorption of water and inorganic salts through the epithelium into the vessels of the lamina propria of its mucosa (1). Gall bladders are one of the more frequently encountered specimens in the surgical pathology laboratory. They are usually removed for stones and/or inflammatory conditions, but rarely may they harbor a neoplasm. Gall stones are a major cause of morbidity and mortality throughout the world. Cholecystectomy is the means by which the pathologist can diagnose the most common pathology of the gall bladder, which is chronic cholecystitis typically accompanied by cholelithiasis. By studying the histopathological changes the pathologist can diagnose chronic cholecystitis, which is typically accompanied by cholelithiasis. About 10% of the adults have gallstones (2,3). There is a female to male ratio of about 2 to 1 in the younger age groups, and with advancing age there is increasing prevalence in females. After the age of 60 yrs about 10 to 15 % of men and 20 to 40 % of women have gall stones (2). The risk of gall stones is also associated with a history of childbearing, estrogen replacement therapy, oral contraceptive use and marked obesity. The peak incidence is in the 5th and 6th decades. For the patient with cholecystitis the preoperative diagnosis is most commonly chronic cholecystitis in 70% to 80% of cases, followed by acute cholecystitis in 20% to 30%

Corresponding author: Major(Dr) Mohan Angadi
Assistant Professor, Department of Anatomy, Armed Forces Medical College (AFMC), Pune-411040

of cases (4). The surgical specimen removed for chronic cholecystitis is associated with cholelithiasis in about 95% cases. Chronic cholecystitis may follow in the wake of single or recurrent attacks of acute cholecystitis. The overwhelming majority of cholecystectomies are performed for symptomatic cholelithiasis with biliary colic related to intermittent obstruction of gall bladder neck and/ or cystic duct by gall stones (4).

The gall bladder is a pear shaped saccular structure located in a depression on the inferior surface of the right and quadrate lobes of liver known as gallbladder bed. Its normal dimensions in adults vary and are dependent on the volume of bile contained within; the gallbladder may be up to 10 cm long, 4 cm wide, and have a wall thickness of 1mm to 2mm. The blind end that projects beyond the anterior liver margin is known as fundus. Most of the organ is formed by central body, a portion of which bulges toward the upper margin of the first portion of the duodenum forming the infundibulum, or Hartmann's pouch. The neck is short and narrow segment located between the body and cystic duct (5). Gall bladder is attached to the liver by loose connective tissue that contains blood vessels, lymphatics, and occasionally bile ducts. A peritoneal fold known as the "Cholecystoduodenal ligament" attaches the infundibulum to the first portion of the duodenum (6). The wall of the gallbladder has three layers: mucosa, muscularis, and adventitia. The mucosa composed of surface epithelium and lamina propria, projects into the lumen as branching folds that increase in height as the gallbladder contracts and are less prominent in the distended organ. Three types of epithelial cells are normally found in the mucosa: columnar, "pencil-like" and basal. A single layer of columnar cells, with basally oriented nuclei, forms the surface epithelium. This cell has a lightly eosinophilic cytoplasm and a few small apical vacuoles. Ultrastructural examination shows short microvilli projecting into the lumen. Invaginations of the apical portions of the luminal cell membrane give rise to pinocytic vesicles. These cells are tightly joined together by apical junctional complexes. The lateral membranes of the neighboring cells interdigitate and surround an extracellular space, the width of which varies according to the content of water and electrolytes actively transported into it. The "pencil-like" cell, occasionally seen in the surface epithelium, is a narrow columnar cell with dark eosinophilic cytoplasm. This cell is not a squeezed or compressed columnar cell, since ultrastructurally it contains more organelles and shows basal cytoplasmic extensions that penetrate the basement membrane (6).

The basal cell is a rarely observed type of epithelial cell found in contact with and parallel to the basement membrane. In addition to the epithelial cells, a few T-lymphocytes are normally present between the surface columnar cells (5). Several tubulo-alveolar glands are present in the neck of the normal gall bladder. These mucous glands are composed of low columnar or cuboidal cells with clear cytoplasm and basally located nuclei. These glands are exclusively located in the neck, since when glands with a similar appearance are seen elsewhere they usually represent pyloric gland metaplasia (5). Rokitansky-Aschoff sinuses describe the pathologic herniations of the mucosa into or through the muscularis. Enfoldings of the mucosa in the lamina propria are common in the contracted gallbladder and should not be regarded as abnormal. The lamina propria is composed of loose connective tissue, nerve fibers, blood vessels, IgA – containing plasma cells, mast cells, and macrophages may be present. The muscular layer is a slightly thickened version of the muscularis mucosa of the intestine composed of bundles of loosely arranged smooth muscle separated by fibrovascular connective tissue. The adventitia is composed of loose connective tissue, blood vessels, lymphatics, nerves, and fatty tissue. Its abdominal side is covered by serosa. Rare paraganglia may be seen adjacent to the vessels. On the hepatic side Luschka ducts may be seen in the adventitia. These small, usually microscopic, bile ducts may be solitary or multiple and are lined by cells similar to those of the intrahepatic bile ducts. Larger accessory biliary ducts may occasionally be present in the adventitia. Leakage of bile into the peritoneum may occur if these ducts are left patent after a Cholecystectomy. The extrahepatic bile ducts are lined by a single layer of tall columnar cells that, except for containing less mucin, are otherwise similar to those present in the gallbladder. The epithelium invaginates into the stroma, forming pockets or pits called "sacculi of Beale." On tangential sections, they may deceivingly appear as deep glands unconnected with the surface epithelium. It is through these saccules that the secretions produced by the biliary glands drain. These unevenly distributed glands have a lobular arrangement and are surrounded by dense stroma. They are lined by mucin producing low columnar to cuboidal cells. The stroma beneath the surface epithelium is dense and contains very few inflammatory cells (6). Cholelithiasis produces diverse histopathological changes in gall bladder mucosa namely acute inflammation, chronic inflammation, cholesterosis, dysplasia and carcinomatous changes. The wall of the gall bladder is thickened often with fibrous adhesions. The mucosal pattern is completely disrupted, sometimes focally ulcerated adjacent to stones, often with constricting inner folds or focal broad outpouchings of the lumen. Chronic inflammatory cells infiltrate the wall and consist of lymphocytes, plasma cells, and histiocytes, with the lymphocytes predominating. Rokitansky- Aschoff sinuses are a characteristic feature of chronic cholecystitis occurring in many cases, and are outpouchings of mucosal epithelium into and through the muscularis coat (7).

A variety of metaplastic changes may be present, including intestinal metaplasia with the appearance of goblet cells at the tip of mucosal folds, and with more development there may be a variable proportion of goblet cells, columnar cells with a brush border, Paneth cells and endocrine cells. It has been estimated that 50% of gall bladders with chronic inflammation may exhibit hyperplasia of pyloric type glands, which are usually confined to the lamina propria but have been described extending into the muscular layer and subserosa.(4).

MATERIALS AND METHODS

Fifty gall bladders were collected for this study from two general hospitals. These comprised of Cholecystectomy specimens obtained from patients who had undergone open/ laparoscopic Cholecystectomy. All these patients were cases

of either cholelithiasis or clinically suspected cases of cholecystitis. The gall bladders obtained at autopsy in these hospitals were excluded from the study. Also, the potentially infectious cases like AIDS, Hepatitis B, bone marrow recipients, and patients receiving multiple transfusions, patients receiving parenteral nutrition were also excluded from the study. The gall bladders obtained for the study were from both male and female patients in the age group of 20 to 90 years. The gall bladders were utilized for studying the gross anatomy as well as the histology in cases of cholecystitis. This facilitated the comparison and correlation of its histological structure with its gross features. However, the analysis chemical composition of gall stones was not undertaken in our study. The structural anatomy of the gall bladder is straightforward being a saccular structure with one end that narrows to form cystic duct, but it has two very different external surfaces. It is important to differentiate between the two surfaces. The smooth surface is lined by peritoneum. In contrast, the rough surface is where the adventitia of gall bladder has been dissected from the undersurface of the liver, and it represents surgical margin. The lymphatics of the gall bladder drain into a lymph node that is located along the cystic duct. When present in the specimen, this lymph node can be identified by palpating the soft tissues investing the cystic duct (32).

The gall bladder specimens were received as cut open specimen but in small number of cases the specimen was received as intact specimen. In cases of intact specimens the gall bladder was opened lengthwise through the serosal-lined surface. This was done by using a small pair of scissors, beginning at the fundus, and extending the incision through the body and neck of the gall bladder and then through the cystic duct. After opening the specimen, the contents of the gall bladder and the cystic duct were noted. The calculi were specifically looked for in the intact specimens. The locations of calculi were noted, whether within the lumen of gall bladder or within the cystic duct.

The thickness of the gall bladder wall and the appearance the mucosa were also noted. If the neoplasm was suspected by the presence of an exophytic lesion, then the external adventitial was inked as this represented a surgical margin. The gall bladder was sampled after fixation. The histology of gall bladder was studied by one representative full thickness section passing from the fundus and one transverse section through the neck of gall bladder (Diagram 1). Additional sections were taken in case of focal lesions and otherwise when required. These sections were kept in vials, each containing 20 ml of 10% buffered formalin for 5- 7 days. An identifying label was pasted on each vial. The tissue was allowed to fix for 24 hrs before it was taken for grossing. The sections were dehydrated by passing it through upgraded strength of alcohol. The dehydrating agents were removed from the tissue by process of clearing using chloroform. After clearing, the tissue was embedded in paraffin wax (melting point 60 degree Celsius) using Leuckhart's moulds. Sections of 3 to 5 microns were taken with the help of Rotary Microtome. The ribbons so formed were dipped in alcohol and floated on a tissue floatation bath maintained nearly at 50 degree Celsius. Each section was fished on a slide primed with egg albumin and thereafter incubated overnight at 37 degree Celsius for smooth removal of wax. This slide was stained with haematoxylin and eosin, and then examined under the microscope.

RESULTS

Analysis

The interpretation of the abnormal histological findings was done under the guidance of an experienced pathologist. Sample of histopathology report used in our study is attached as per **Annexure-I.** The data pertaining to patient's particulars and histopathological results is attached as per **Annexure-II.**

Table 1. Age distribution of patients in our study

Serial No	Age group (in Yrs)	No	Percent (%)
1	<20	1	2
2	21-30	8	16
3	31-40	8	16
4	41-50	13	26
5	51-60	11	22
6	61-70	7	14
7	71-80	1	2
8	>80	1	2

Table 2. Sex distribution of patients in our study

Serial No	Age group (in Yrs)	No	Male	Female
1	<20	1	1	0
2	21-30	8	3	5
3	31-40	8	3	5
4	41-50	13	6	7
5	51-60	11	2	9
6	61-70	7	2	5
7	71-80	1	0	1
8	>80	1	0	1

Table 3. Results of Cholecystectomy in 50 Patients with Clinically evident Cholecystitis in our study

Serial No	Histologic finding	Number (%)
1	Chronic Cholecystitis	44(88%)
2	Chronic Cholecystitis with Cholesterolosis	1(2%)
3	Chronic Cholecystitis with intestinal metaplasia	1(2%)
4	Adenocarcinoma	1(2%)
5	Xanthogranulomatous Cholecystitis	1(2%)
6	Normal findings	2(4%)

Table 4. Sex distribution of Patients showing Chronic Cholecystitis in our study

Serial No	Sex	No	Percentage
1	Males	16	36.3%
2	Females	28	63.7%

Table 5. Comparison of histological findings in various International studies

	Csendes *et al.*	Barcia	Zahrani & Mansoor	Hopwood *et al.*	Present study
Chronic Cholecystitis	100%	75%	97%	90%	88%
Carcinoma	Not reported	Not reported	1%	Not reported	2%

Table 6. Comparison of histological findings in various Indian studies

	Baig *et al*	Mohan *et al*	Tyagi *et al*	Present study
Chronic Cholecystitis	80%	82.2%	50.8%	88%
Carcinoma	2.5%	1.09%	6.8%	2%

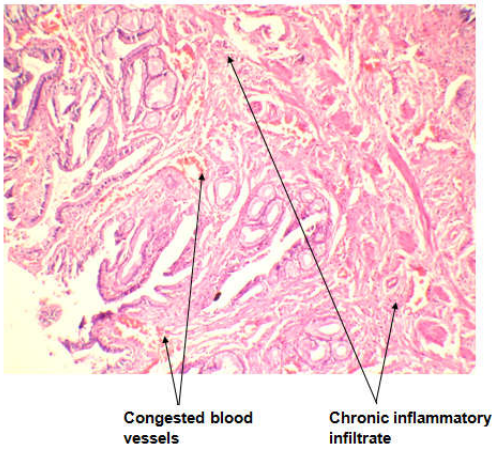

Fig 1.1 Chronic Cholecystitis showing chronic inflammatory infiltrate and congested blood vessels.10X

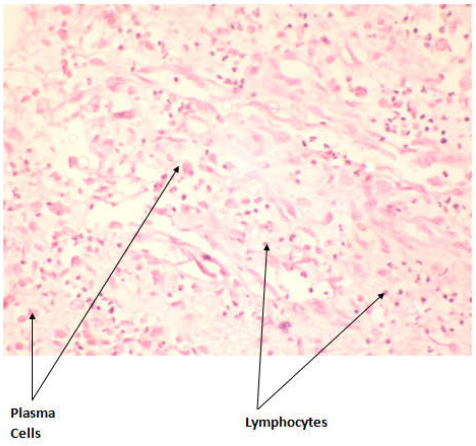

Fig 1.2 Chronic inflammatory infiltrate in Chronic Cholecystitis showing lymphocytes and plasma cells. 40X

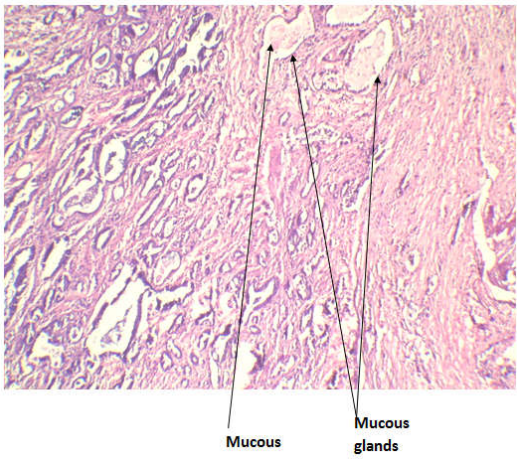

Fig 4.1 Congested mucous glands filled with mucous in Muscularis propria suggestive of Adenocarcinoma. 10X

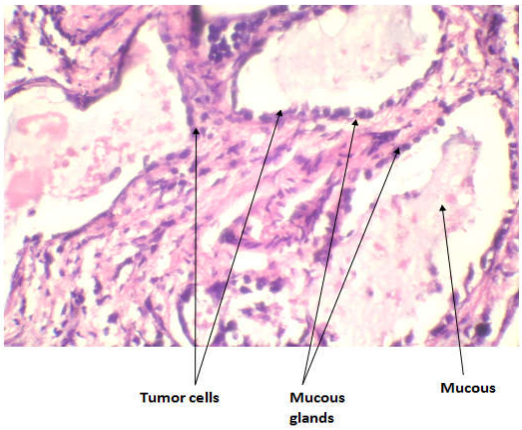

Fig 4.2 Mucous glands lined with tumor cells showing high nuclear cytoplasmic ratio, nuclear atypia, hyperchromatic nucleus and mild eosinophilic cytoplasm.40X

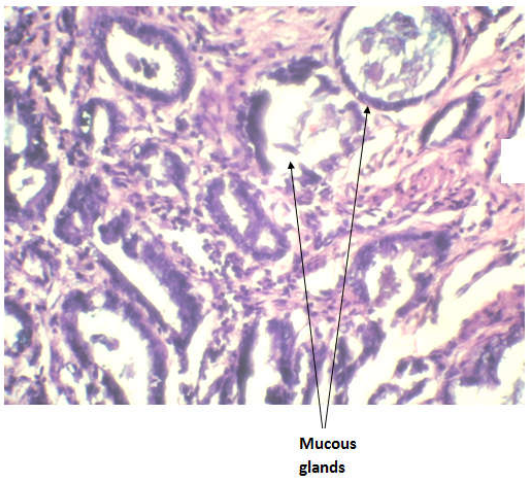

Fig 4.3 Congested mucous glands filled with mucous in muscularis propria suggestive of Adenocarcinoma. 40X

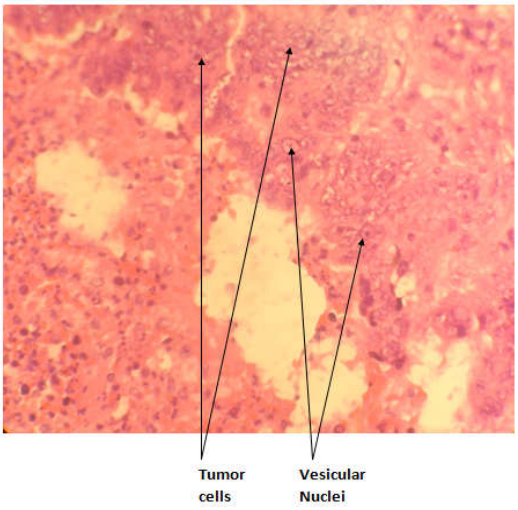

Fig 4.4 Adenocarcinoma showing clusters of tumor cells with high nuclear cytoplasmic ratio, nuclear atypia, hyperchromatic nucleus

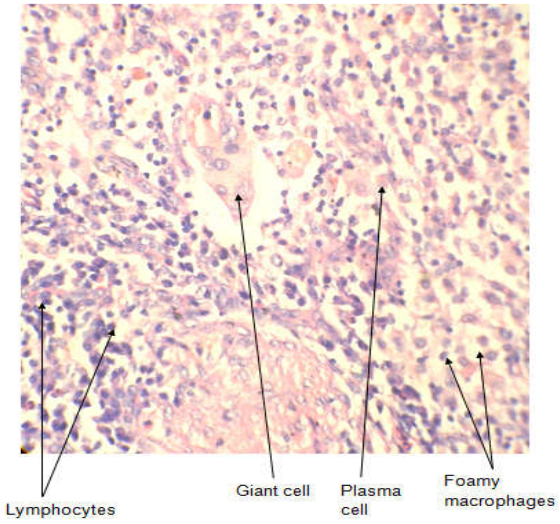

Fig 5.1 Xanthogranulomatous cholecystitis showing large number of foamy macrophages involving the lamina Propria. Few multinucleated giant cell are also seen along with numerous lymphocytes and plasma cells. 40X

DISCUSSION

The diverse spectrum of histopathological findings of gall bladder has remained an enigma for the pathologists, which has led various workers to study it from time to time. In our present study an endeavor has been made to present an account of generally accepted views and to observe and compare the differences. Csendes A in his study on histological findings in gall bladder mucosa showed that out of 95 control subjects 33% cases showed abnormal histological findings, mainly chronic cholecystitis, which increased with age and was frequently seen among women. He also reported that all 80 patients with asymptomatic gallstones showed chronic cholecystitis and/or Cholesterolosis. His findings suggest that chronic inflammatory changes can occur in the gall bladder prior to the appearance of macroscopic stones (50). The findings of our study showed chronic cholecystitis as the predominant finding in forty four cases accounting to 88% of the total cases. There was a female preponderance with twenty eight cases showing the findings of chronic cholecystitis in our study. These findings were in corroboration with observations of Csendes A who also showed that chronic cholecystitis was the predominant finding and was frequently seen in woman. Similar findings were observed by Badke A in a retrospective study of 1101 patients with symptomatic cholelithiasis observed inflammatory changes in gall bladder in 96.7%, chronic fibrotic cholecystitis in 94.5% and a severe form of cholecystitis in 8.8% cases (52). D Hopwood in his study titled "Cholecystitis: A fine structural analysis" reported that 90% cases had cholecystitis with associated cholelithiasis (53). Our study was in corroboration with D Hopwood with 86% cases showing the histopathological findings of chronic cholecystitis. Tyagi SP *et al* studied morphological changes in 415 cholecystectomy cases at Department of Pathology, Jawahar Lal Nehru Medical College, Aligarh Muslim University and observed the following (54)

"There was a preponderance of females (male to female ratio--1:6.5). The mean age of the cases was 43.6 years. Most of the cases (63.4%) were in the 4th and 5th decades of life. The average duration of illness was 2.8 years. Associated cholelithiasis was present in 85.3% cases. Gall-stones were of mixed variety in 78.2% cases, cholesterol type in 15.3% cases and both types were present in 6.5% cases. Chronic cholecystitis was the main histological diagnosis (50.8%). Other lesions observed were adenomyomatosis (8.2%), adenomatous hyperplasia (10.1%), granulomatous cholecystitis (4.1%), cholesterosis (2.7%), acute cholecystitis (4.1%), acute on chronic infection (10.8%), sub-acute cholecystitis (2.4%) and carcinoma gall bladder (6.8%). The frequency of Rokitansky-Aschoff's sinuses was closely related with the degree of inflammatory response. In 13 (6.2%) cases the diagnosis of chronic follicular cholecystitis was made. All the cases of cholesterosis were multiparous females and of younger age. Of the malignant lesions, adenocarcinoma was the commonest (96.4%)."

Baig SJ in his study titled "Histopathological changes of gall bladder mucosa in cholelithiasis: Co-relation with chemical composition of all stones" reported the following observations (55). "Out of 40 patients (n = 40) 29 were females and 11 were

males. The mean age of our patients was 38 +/- 21 years with a median of 40 years. Median age of males was 48 years compared to 38 years for females. Twenty-eight patients had mixed stones, 8 had pigment stones and 4 had cholesterol stones. Out of 28 patients with mixed stones 14 had histological picture of chronic cholecystitis, 8 had granulomatous cholecystitis, 4 had adenomatous hyperplasia, 1 had dysplasia and 1 had carcinoma. All 8 patients having pigment gallstones had chronic cholecystitis. Out of 4 patients with cholesterol gallstones, 2 had chronic cholecystitis, 1 had adenomatous hyperplasia and 1 had cholesterosis. Gallbladder having pigment stones were devoid of Rokitansky-Aschoff sinuses." Mohan *et al* studied the spectrum of gall stone disease in North India At the Departments of pathology and Surgery, Government Medical College and Hospital, Chandigarh, India and reported the following (56). "There was a preponderance of females (M: F ratio 1: 6.4). The age of the patients varied from 10 to 90 years with maximum number of cases between 31 and 40 years of age. On morphological analysis, gallstones were of mixed type in 686 cases (62.3%), pigment type in 34 cases (3.2%), cholesterol type in 182 cases (17.3%), and combined type in 148 cases (14%). Other lesions associated with chronic cholecystitis were cholesterolosis in 112 cases (10.1%), xanthogranulomatous cholecystitis in 26 cases (2.3%), follicular cholecystitis in 26 cases (2.3%), ceroid granulomas in ten cases (0.9%), eosinophilic cholecystitis in six cases (0.5%), and carcinoma in 12 cases (1.09%). Maximum number of carcinomas was associated with pigment stones, that is, 7 out of 12 cases (58.3%)."

Barcia JJ in his study reported Chronic Cholecystitis in 75% of cases with epithelial metaplasia and 73% with regenerative epithelium, the latter being associated with erosion but not with presence of cholelithiasis (57). A histopathological study in the Ethiopian population done by Bekele and Tegegn showed that chronic cholecystitis was a common disease in Ethiopia, with 93.5% calculus and 6.5% acalculus cases. (51). Similar findings were observed in a study by Zahrani & Mansoor in Saudi population which showed that benign lesions comprised 99%, mostly chronic Cholecystitis (97%), acute cholecystitis (2%), and malignant lesions comprised only 1% of all lesions (58). The findings of our study were in agreement with Zahrani & Mansoor with chronic cholecystitis as the predominant finding and malignant lesions being comparatively rare with only one case of adenocarcinoma being reported in our study. In a study of spectrum of gall bladder disease in Indian population, Mohan H reported that the pathological findings showed that Cholesterosis was present in 26.3% of cases with cholesterol cholelithiasis, and 6.8% of cases with mixed cholelithiasis. Also, male to female ratio observed in this study was 1:6.4(56). Cholesterolosis refers to the accumulation of neutral lipid, particularly cholesterol esters and triglyceride, within macrophages in the lamina propria of gall bladder. The disorder is relatively common. In his book tilted "Pathology of the Pancreas, Gall Bladder, Extrahepatic biliary Tract and Ampullary region" Ernest E Lack reported a variable incidence ranging from 8.8% and 39% in separate studies. It is most common over the age of 40 years, with most cases occurring in the 5th and 6th decades (4). However, in our study 2% cases showed changes of cholesterolosis associated with chronic cholecystitis. Our study was carried on the surgically removed gall bladder specimens in patients of cholelithiasis and clinically diagnosed cholecystitis excluding the autopsy cases. This could be a possible reason for the low percentage of cholesterolosis reported in our study as compared to the report of Ernest E Lack Who studied both the surgical and autopsy cases. One case showed Xanthogranulomatous cholecystitis in our study. The changes are characterized by the extensive presence of foamy macrophages which are laden with cholesterol esters and triglycerides in the lamina propria. There is a mixture of different cells, but the predominant cells are foamy macrophages. Lymphocytes and plasma cells are also present. Sometimes multinucleated giant cells are present, along with occasional cholesterol clefts. These changes are often accompanied by some fibrosis, and plump spindle cells may align in a vague storiform arrangement (4). In our study foamy macrophages typical of Xanthogranulomatous cholecystitis were seen along with lymphocytes and plasma cells in the lamina propria. Few giant cells were also seen (Fig 5.1).

One case showed changes suggestive of Adenocarcinoma of gall bladder in our study in a 88 year old female. Carcinoma of gall bladder is the fifth most common malignancy of the gastrointestinal tract. It is disorder primarily of the elderly being more frequently found in women. 98-99% of gall bladder malignancies are carcinomas and 75-90% of these are pure adenocarcinomas. Benign neoplasms of the gall bladder are rare and the reports are confused by the inclusion in some reports of cholesterol polyps and the fundal collections of Rokitansky- Aschoff sinuses referred to as adenomyomas or localized adenomyomatosis, neither of which are neoplasms(49). Most invasive carcinomas of gall bladder and extrahepatic bile ducts are preceded by dysplasia and carcinoma in situ. These are often seen in association with cholelithiasis, and they usually arise in an abnormal mucosa showing pyloric gland and intestinal metaplasia. Dysplasia and carcinoma in situ usually begin on the surface epithelium and extend laterally and downward as Rokitansky-Aschoff sinuses and metaplastic glands. Dysplasia is characterized by columnar or cuboidal cells with or without stratification, nuclear enlargement and hyperchromatism, prominent nucleoli, loss of polarity, and mitotic figures. In carcinoma in situ these changes are more pronounced than in dysplasia and a cribriform architecture may be present. The distinction between severe dysplasia and carcinoma in situ is often subjective and sometimes impossible (6). Only a small proportion of invasive tumors arise from preexisting adenomas.

In two cases no gall stones were found on gross examination, but on histological examination, these cases showed changes of chronic cholecystitis. These were not grouped as a separate entity because the histological changes were the same as chronic cholecystitis. This finding was in corroboration with Mohan H *et al* who reported that in 50 cases out of 1100 cases studied (4.5%), there were no gallstones, but on histological examination all these cases too showed changes of chronic cholecystitis (56). Few lymphocytes were seen in the lamina propria in these cases. These were reported as histologically normal gall bladders. This was also in agreement with the observations of Csendes A that chronic inflammatory changes

can occur in the gall bladder prior to the appearance of macroscopic stones. Bekele and Tegegn in their study on the Ethiopian population also reported 6.5% acalculus cases showing the findings of chronic cholecystitis (51). In another study Aihara N *et al* found Acalculous cholecystitis as a relatively rare condition occurring in critically ill patients or as a postoperative complication following surgery unrelated to the biliary tract (60). A variable incidence of Acalculus cholecystitis has been reported in certain clinical conditions such as during and after hyperalimentation, the post operative period, multiple transfusions, sepsis, and bone marrow recipients and AIDS patients (8, 9, 10,13). However, in our study we excluded all these potentially infected cases, bone marrow recipients and patients receiving multiple transfusions. The gross and histological findings in our study were in corroboration with other studies done on the subject (Table 5, Table 6). However, our study was not in agreement with Tyagi SP, who reported 50.8% cases of chronic cholecystitis and 6.8% cases of carcinoma in his study one on a cross section of North Indian population. Though there was general agreement on the predominant finding being chronic cholecystitis but there was considerable difference in the percentage of reported cases. There was a definite co-relation with cholelithiasis to cholecystitis with chronic cholecystitis being the predominant histological finding seen. This predominance of chronic cholecystitis was confirmed in comparison with other International (Table 4) and Indian studies (Table 5). We could not establish a definite relationship between chemical nature of gall stones and the histological findings seen because the chemical composition of gallstones was not included in our study. There was a preponderance of females showing chronic cholecystitis as a predominant finding in cholelithiasis. The only case of Adenocarcinoma diagnosed in our study was an 88 year old female. This is similar to the other studies done by various workers on the subject who reported increased incidence of adenocarcinoma in females with advancing age (49, 56).

Two cases of clinically evident cholecystitis without cholelithiasis showed normal histological findings amounting to 4% of total cases. Csendes A, who in a study of histologic findings of gallbladder mucosa in 87 patients with morbid obesity without gallstones compared to 87 control subjects reported normal gallbladder mucosa in 28.7% of obese women compared to 34.2% of control women ($P > 0.59$), with similar findings among the men. Also in comparison of population of obese patients to control subjects, a similarly high proportion of histologic abnormalities of the gallbladder mucosa were found in the absence of stones (61). In another study titled "Chronic acalculous cholecystitis: laparoscopic treatment", Jones *et al* reported normal histological findings in 6% of cases. In this regard our study was more in agreement with Jones *et al*. However, high proportion of cases with normal histology as reported by Csendes was essentially a study aimed at finding the histological abnormalities of gall bladder in obese patients in comparison to the control cases. This could be the reason for reason for high proportion of normal histological findings reported by Csendes. Moreover, due to high prevalence of gall stones in the Chile and other Scandinavian countries, it is also possible that high numbers of cholecystectomies are being done and sent for histopathological examination. This difference of reported cases necessitates further studies. Other rare entities like eosinophilic cholecystitis, Vasculitis, sarcomas, non neoplastic polyps, hydrops and mucocele were not reported in our study.

Conclusion

About fifty gall bladder specimens were utilized for the histopathological study. These cases had undergone Cholecystectomy either for cholelithiasis or clinically suspected cases of chronic cholecystitis with the age of patients ranging from 18 to 88 years. The definitive diagnosis was established by ultrasound preoperatively. The gall bladders were studied for both gross and histopathological changes under light microscope using haematoxylin and eosin stains.

The following were observed:

Gross findings

1. The cut section of the gall bladders received in the histopathological lab showed velvety, bile stained mucosa, congested serosa and thickened wall in all the forty four cases of chronic cholecystitis and sole cases of cholesterolosis and intestinal metaplasia. Sole case of adenocarcinoma showed an irregular, firm growth measuring about 0.8cm to 0.5 cm at the junction of neck and fundus and markedly thickened wall. Xanthogranulomatous cholecystitis case showed thick wall and congested mucosa.
2. Gall stones were present in forty eight cases comprising 96% of the total cases under study. The chemical composition of different types of gall stones was excluded in the study.
3. Chronic cholecystitis was associated with cholelithiasis in forty two cases. In the remaining two cases, no gall stones were found on gross examination but showed histopathological changes suggestive of chronic cholecystitis.

Microscopic

1. The mucosal changes in all the forty four cases of chronic cholecystitis showed marked thickening, presence of chronic inflammatory infiltrate containing predominantly lymphocytes and presence of proliferating fibroblasts. Single case of adenocarcinoma diagnosed in our study also showed marked thickening of mucosa. Two cases showed normal mucosa with few lymphocytes.
2. All the forty four cases of chronic cholecystitis in our study showed the chronic inflammatory infiltrate in the lamina propria. Only case of adenocarcinoma showed congested glands filled with mucous in the lamina propria.
3. The muscularis propria showed chronic inflammatory infiltrate with the lymphocytes predominating in all cases of chronic cholecystitis and sole case of adenocarcinoma. Adenocarcinoma case also showed congested glands filled with mucous extending from the lamina propria to the muscularis propria.
4. Only case of Xanthogranulomatous cholecystitis reported showed marked inflammatory infiltrate in lamina propria

and muscularis propria with predominance of foamy histiocytes. Other cells seen in these cases were the lymphocytes and plasma cells.

5. The adenocarcinoma case showed the extension of chronic inflammatory infiltrate through the muscularis propria and reaching the serosa. The congested mucous glands were seen reaching the serosa.

In conclusion, Cholecystectomy specimens operated for cholelithiasis and clinically evident chronic cholecystitis present diverse histological abnormalities which remain a dilemma to histopathologists due to close resemblance among themselves. The available literature reports close similarities between Xanthogranulomatous cholecystitis, adenocarcinoma and chronic cholecystitis (28, 29). Also, a number of variants of chronic cholecystitis have been reported presenting difficulty to the pathologist (56). The importance of correct histopathological diagnosis is especially important for the postoperative management of adenocarcinoma. A number of cases of acalculus cholecystitis has been reported in certain clinical conditions such as during and after hyperalimentation, the post operative period, multiple transfusions, sepsis, and bone marrow recipients (8,9,10). Rare cases of Acalculous cholecystitis have also been reported from AIDS patients due to cryptosporidiosis (13). French *et al* in his study on 107 AIDS patients observed that 93% of resected gall bladders showed evidence of cholecystitis; 73% of cases were Acalculous; and 53% of these were idiopathic. This study also showed that opportunistic infection was found in nearly 40% of all cases. Histopathological findings were more marked in gall bladders demonstrating cytomegalovirus showing mucosal erosions and deep ulcers were. In other studies, Candida albicans and Mycobacterium avium complex have also been demonstrated (5). Acalculous cholecystitis has also been reported in the MEN type IIB syndrome with ganglioneuromatosis of the alimentary tract, including gall bladder (12). However we have excluded such potentially infectious cases, bone marrow recipients, patients receiving multiple transfusions from our study.

Chronic cholecystitis is the predominant histological abnormality seen in 88% of cases in our study which is in accordance with the reported incidence of chronic cholecystitis in most of the published literature in both International and Indian studies (Table 5, Table 6).

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ANNEXURE – I

HISTOPATHOLOGY REPORT

Hospital		Ward:		Biopsy No:			
No:		Rank:		Name:			
Unit		Age		Sex		Previous Ref:	
Clinical Diagnosis:							
Nature of specimen:							
Date of biopsy:		Date of receiving:		Date of grossing:			
Gross:							
Microscopic:							
Opinion:							

ANNEXURE-II

HISTOPATHOLOGY RESULTS

S.No.	Biopsy no	Age	Sex	Diagnosis
1	1	21	M	Chronic cholecystitis
2	2	28	M	Chronic cholecystitis
3	3	64	M	Chronic cholecystitis
4	4	26	F	Chronic cholecystitis
5	5	45	F	Chronic cholecystitis with Cholesterolosis
6	6	28	M	Chronic cholecystitis
7	7	56	F	Chronic cholecystitis
8	8	61	F	Chronic cholecystitis
9	9	88	F	Adenocarcinoma
10	10	44	F	Chronic cholecystitis
11	11	42	F	Chronic cholecystitis
12	12	40	F	Chronic cholecystitis
13	13	55	F	Chronic cholecystitis
14	14	42	F	Chronic cholecystitis with intestinal metaplasia
15	15	36	F	Chronic cholecystitis
16	16	52	F	Chronic cholecystitis
17	17	56	F	Chronic cholecystitis
18	18	48	M	Chronic cholecystitis
19	19	28	F	Chronic cholecystitis
20	20	47	M	Chronic cholecystitis
21	21	60	F	Chronic cholecystitis
22	22	64	F	Chronic cholecystitis
23	23	39	M	Chronic cholecystitis
24	24	55	F	Chronic cholecystitis
25	25	35	M	Chronic cholecystitis
26	26	43	F	Chronic cholecystitis
27	27	25	F	Chronic cholecystitis
28	28	70	F	Chronic cholecystitis
29	29	62	F	Chronic cholecystitis
30	30	46	M	Chronic cholecystitis
31	31	75	F	Chronic cholecystitis
32	32	60	F	Normal gall bladder
33	33	30	F	Chronic cholecystitis
34	34	52	F	Chronic cholecystitis
35	35	35	F	Chronic cholecystitis
36	36	35	F	Chronic cholecystitis
37	37	42	M	Chronic cholecystitis
38	38	54	F	Normal gall bladder
39	39	62	M	Chronic cholecystitis
40	40	40	M	Chronic cholecystitis
41	41	45	F	Chronic cholecystitis
43	43	58	M	Chronic cholecystitis

S.No	Biopsy No	Age	Sex	Diagnosis
44	44	32	F	Chronic cholecystitis
45	45	57	M	Chronic cholecystitis
46	46	64	F	Chronic cholecystitis
47	47	18	M	Chronic cholecystitis
48	48	30	F	Chronic cholecystitis
49	49	43	M	Xanthogranulomatous cholecystitis
50	50	45	F	Chronic cholecystitis

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