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Article Review

Histopathological Mucosal Change in Chronic Cholecystitis

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بسم الله الرحمن الرحيم

(إِنَّمَا يَخْشَى اللَّهَ مِنْ عِبَادِهِ الْعُلَمَاءُ ۗ إِنَّ اللَّهَ عَزِيزٌ غَفُورٌ)

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إلى من علَّمني كيف أقف بكل ثبات فوق الأرض

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إلى نبع المحبة والإيثار والكرم

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إلى جميع الشهداء رحمهم الله

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الحمد لله ألذي هدانا وأعدنا وأمدنا والهمنا الصبر على المشاق ووفقنا لما نحن عليه

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وارفع كلمة الشكر الى الدكتورة **ذرى عباس**
وفقها الله فقد كانت سندا لنا على طول الطريق

والى كل من مد يد العون لنا من قريب او بعيد

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الى الذين مهدوا لي طريق العلم والمعرفة

الى جميع اساتذتي الافاضل

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Abstract

Gallbladder it is a common cause of abdominal pain due to gallstones.The complication of gallstones included acute cholecystitis, chronic cholecystitis ,etc. Chronic cholecystitis is a chronic inflammation of the gallbladder, typically secondary to gallstones. The chronic cholecystities does not always cause clinical symptoms. The clinical features which can present with chronic cholecystities include dull right upper quadrant pain that radiates to mid back or right scapula. The murphy sign result positive ,Abdominal discomfort often related to fatty food ingestion, Nausea, vomiting, bloating, flatulence. The diagnosis of chronic cholecystities by abdominal ultrasound. Histopathological changes in the gallbladder mucosa results most of the cases showed chronic cholecystitis and its variants followed by acute cholecystitis. Histopathological examination of gallbladder specimens is an important step toward the confirmation of clinical and radiological diagnosis. The treatment of chronic cholecystities is initially conservative treatment following by cholecystectomy . Routine histopathological examination of all gallbladder specimens, regardless of the clinical characteristics of the patient or macroscopic aspect of the gallbladder, is the current approach to detect the presence of gallbladder carcinoma.

Aim: This Article review was carried out to study the diverse histopathological mucosal change in chronic cholecystitis.

Introduction

The gallbladder is a pear shaped organ located in the right upper quadrant of the abdomen. It measures approximately 7-10 cm in length and 4 cm in width. The gallbladder has fundus, a body and a neck that terminates in a narrow infundibulum. The cystic duct joins the gallbladder to the common bile duct, its length is variable, usually ranges from 2-4 cm. The cystic duct is usually 2–3 mm wide. It can dilate in the presence of pathology (stones or passed stones). [1]

The gallbladder stores bile about 30-50 ml and concentration of bile. [2]

The Bile is a digestive fluid which it produced and secreted by the liver is transported by a series of branching bile ducts known as the biliary tree. The several narrow tubular channels, at the cellular level called canaliculi which collect the bile. [1]

The gallbladder epithelium secretes bicarbonate and mucins, which both provide cytoprotection against bile acids. The motor function of gallbladder is regulated by bile acids, and neurohormonal signals linked to digestion, for example, cholecystokinin. [2]

Gallbladder it is a common cause of abdominal pain due to gallstones. Gallstones cause various problems besides simple biliary colic and cholecystitis. With chronicity of inflammation caused by gallstone obstruction of the cystic duct . [1]

Gallstones are classified according to their chemical composition into: cholesterol gallstones, pigment (calcium bilirubinate) gallstones, and mixed gallstones that contain both cholesterol and calcium bilirubinate. [3]

The incidence rates show substantial geographical variation, with the lowest rates reported in African populations. [4]

The etiology of gallstones is probably multifactorial included metabolic, infective, and bile stasis. [2]

Epigastric and right upper quadrant pain occurring 30-60 minutes after meals is frequently associated with gallstone disease. [3]

Classically, the patient will present with right upper quadrant abdominal pain, fever, nausea, vomiting, and an elevated white blood cell count. If the subdiaphragmatic parietal peritoneum is irritated by the inflamed gallbladder, patients may also experience the pain in the right shoulder a phenomenon called referred pain. The complication of gallstones included acute cholecystitis, chronic cholecystitis, gangrene , empyema, perforation, and carcinoma. In the intestine causes acute intestinal obstruction. [1]

Only 30% of patients with asymptomatic cholelithiasis will warrant surgery during their lifetime, suggesting that cholelithiasis can be a relatively benign condition in some people. However, there are certain factors that predict a more serious course in patients with asymptomatic gallstones and warrant a prophylactic cholecystectomy when they are present. These factors include patients with large (> 2.5 cm) gallstones, patients with congenital hemolytic anemia or nonfunctioning gallbladders, or during bariatric surgery or colectomy. [3]

Chronic cholecystitis is a chronic inflammation of the gallbladder, typically secondary to gallstones. The risk factors correspond to those that increase risk of cholelithiasis: female sex, obesity, rapid weight loss, pregnancy, advanced age. The chronic cholecystities does not always cause clinical symptoms. The clinical features which can present include dull right upper quadrant pain that radiates to mid back or right scapula. The murphy sign result positive , Abdominal discomfort often related to fatty food ingestion, Nausea, vomiting, bloating, flatulence. The diagnosis of chronic cholecystities by abdominal ultrasound, Gallbladder wall thickening with associated cholelithiasis, Gallbladder may appear contracted or distended. [5]

The treatment of chronic cholecystities is initially conservative treatment due to preventing complications of inflammation and following cholecystectomy after 6-8 weeks. [3]

The cholesterosis is a non inflammatory alteration of the gallbladder, having as pathophysiology the accumulation of lipids in the wall and the formation of cholesterol polyps, so far without known association with malignant transformation. [6]

The Precancerous changes of gallbladder mucosa (Non- specific pathologies) included Various types of hyperplastic lesions changes can develop in the gallbladder. The first finding was adenomatous hyperplasia of the gallbladder is a condition characterized by a hyperchromatic accentuated fold occure as alterations in epithelium. Macroscopically, this alteration presents in the form of a thick and nodular gallbladder mucosa, particularly in its diffuse form, but it can also produce polypoid lesions. The epithelial surface of the gallbladder and glandular epithelial can undergo focal to diffuse hyperplastic changes. Adenomyomatous hyperplasia is a reactive alteration characterized by hyperplastic and cystic changes in deep parts of the gallbladder mucosa associated with smooth muscle hypertrophy. [5]

The gallbladder epithelium can be subject to various metaplastic changes, including pyloric gland metaplasia, antral gland metaplasia, intestinal metaplasia, and squamous cell metaplasia. Most commen was intestinal metaplasia. [4]

The Variants of chronic cholecystitis included Follicular cholecystitis, Eosinophilic cholecystitis, xanthogranulomatous cholecystitis. The feature of xanthogranulomatous cholecystitis are epithelial indipping into muscle layer as alterations in epithelium, and fibrosis as alterations in Lamina propria. [7]

The dysplasia is a defined as abnormal organization of cells within a specific tissue type ,or disordered intraepithelial proliferation. [8]

Laparoscopic cholecystectomy it’s a gold standard in the treatment of symptomatic gallstones. In recent years, early laparoscopic cholecystectomy has become more common. [3]

Cholecystectomy performed for benign diseases of the gallbladder is important for the diagnosis of gallbladder cancer. This is done by pathological examination of the removed specimens for patients with no detected or suspected complications before surgery. Histopathological examination of gallbladder specimens is an important step toward the confirmation of clinical and radiological diagnosis. [9]

Review Article

1-Chronic inflammation.

In the study of Amandeep Singh, Guramritpal Singh, and Deepika Sharma, etal. the predominant comprising chronic cholecystities in 79% from 100 cases ,the female number were 85 and the male number were 15. Majority of the patients were in age group of 40–49 years [4]. IN the study of Gyanaranjan Nayak, Saurjya Ranjan Das, Biswa Bhusan Mohanty, Pratima Baisakh ,etal .The gallbladder specimens were collected from 70 cases, (49 females and 21 males) ,most of cases show chronic cholecystitis in incidence 64.5% [7]. Another related study that was done by Ana Karolina Gama Holanda, Zailton Bezerra Lima Júnior. The registered reported histopathological exams of 2 in 1278 pts , 992 were from females and 286 from males. The mean age was 43±17.8 years .The most common pathological finding was chronic cholecystitis, present in frequency 97.8% [10]. In my opinion, the researchers of ana group took many more patients than amandeep group and Gyanaranjan group, And also a variety of age from young people to the elderly, so the result was more.

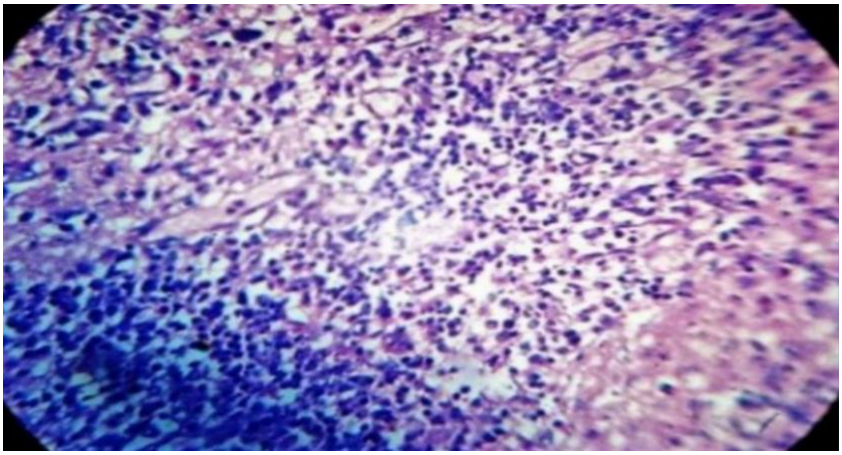

Figure 1: Inflammatory infiltrate found in cholecystitis.

2-Acute inflammation.

In the study of Mohamed Benkhadoura, Akrem Elshaikhy, and Osama Elfaedy, etal. The registereds reported histopatholoical examination of gallbladder specimens in 3423, the males number were 486 (14.2%), and the females were 2937 (85.8%).Median age of the patients was 40 (14-93) years. The result was found in 237 pts of acute cholecystitis in frequency (6.9%) [11]. Another related study that was done by Dr- T.Pavlidis, C-Lazaridis, K-Atmazidis, J-Makris, B-Papaziogas, T.Papaziogas ,and etal. A total of 3677 patients included 2758 women 75% and 919 men 25%. The mean age was 57 years (range 21 to 93 years), and 915 patients were older than 65 years. The result was found in 119 pts of acute cholecystitis in frequency (5.8%) [12]. Finally, we have the study of Gyanaranjan Nayak, Saurjya Ranjan Das, Biswa Bhusan Mohanty,etal. The gallbladder specimens were collected from 70 cases of elective cholecystectomy, the patients included (49 females and 21 males),The frequency of acute cholecystitis was (10%) [7]. In my opinion, the result of acute cholecystities was high persent in study of Gyanaranjan group, I think this result related to history family and also The collection of all gallbladder specimens was according to the ethical population.

3- Cholesterosis.

The cholesterosis is a non inflammatory alteration of the gallbladder, having as pathophysiology the accumulation of lipids in the wall and the formation of cholesterol polyps, so far without known association with malignant transformation [6].

This pathological finding present in frequency 10.2 %(n=131), In the study that was done by Ana Karolina Gama Holanda , Zailton

Bezerra Lima Júnior,etal [10]. And in frequency 15.5% (n=201), in the study of Oguzhan Dincel, Mustafa Goksu, Hamit Sinan Hatipoglu,etal [6]. And in frequency 17% (n= 347). In the study that was done by Dr- T.Pavlidis, C-Lazaridis, K-Atmazidis, J-Makris, B-Papaziogas, T.Papaziogas ,and etal [12]. I think the similarity of the percentage related to female gender ,is due to the fact that all researchers took samples from women with a number equivalent to four times the number of men , and it has no relationship with age because in all the research the ages were varied from adolescence to old age.

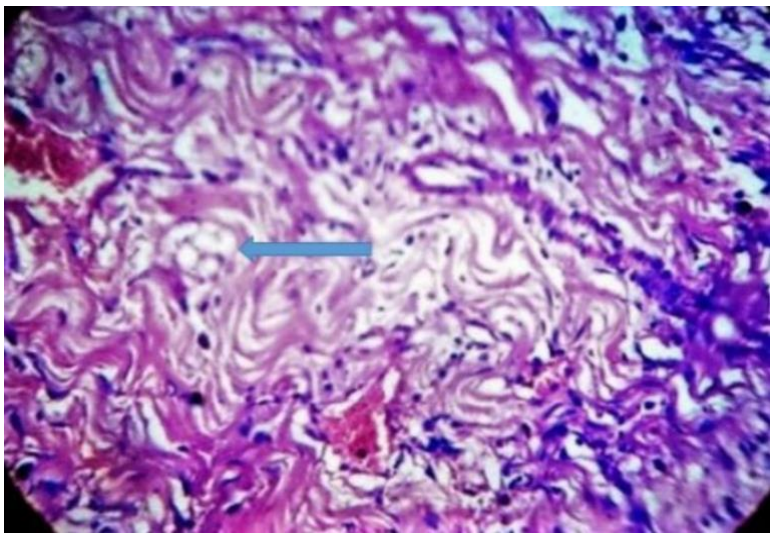

Figure 2: Cholesterolosis, H-Ex40 (Presence of Foamy Macrophages).

4-Precancerous changes of gallbladder mucosa (Non-specific pathologies).

They are importance for both the clinical and pathological examinations. Improved diagnostic procedures allow recognizing invasive carcinoma more frequently at early stage. In the (table 1), We show difference between percentage of each histopathological finding.

Table 1		
Type of histopatholoical change	**Artical Registered**	**N(%)/all pts**
1-Adenomatous hyperplasia	Mohamed Benkhadoura, Akrem Elshaikhy, and Osama Elfaedy, etc.. Oguzhan Dincel, Mustafa Goksu, Hamit Sinan Hatipoglu,etc.	67(2.0)/3423 34(2.6)/1294
2-Inteatinal metaplasia	Oguzhan Dincel, Mustafa Goksu, Hamit Sinan Hatipoglu,etc. Ana Karolina Gama Holanda , Zailton Bezerra Lima Júnior,etc.. Amandeep Singh, Guramritpal Singh, and Deepika Sharma, etc.	39(3)/1294 6(0.5)/1278 1(1.0)/100
3-Xanthogranulomatous	Ana Karolina Gama Holanda , Zailton Bezerra Lima Júnior,etc.. Mohamed Benkhadoura, Akrem Elshaikhy, and Osama Elfaedy, etc.. Amandeep Singh, Guramritpal Singh, and Deepika Sharma, etc.	23(1.8)/1278 4(0.1)/3423 2(2.0)/100
4-Dysplasia	Ana Karolina Gama Holanda , Zailton Bezerra Lima Júnior,etc.. Oguzhan Dincel, Mustafa Goksu, Hamit Sinan Hatipoglu,etc. Mohamed Benkhadoura, Akrem Elshaikhy, and Osama Elfaedy, etc..	13(1.0)/1278 8(0.6)/1294 5(0.1)/3423

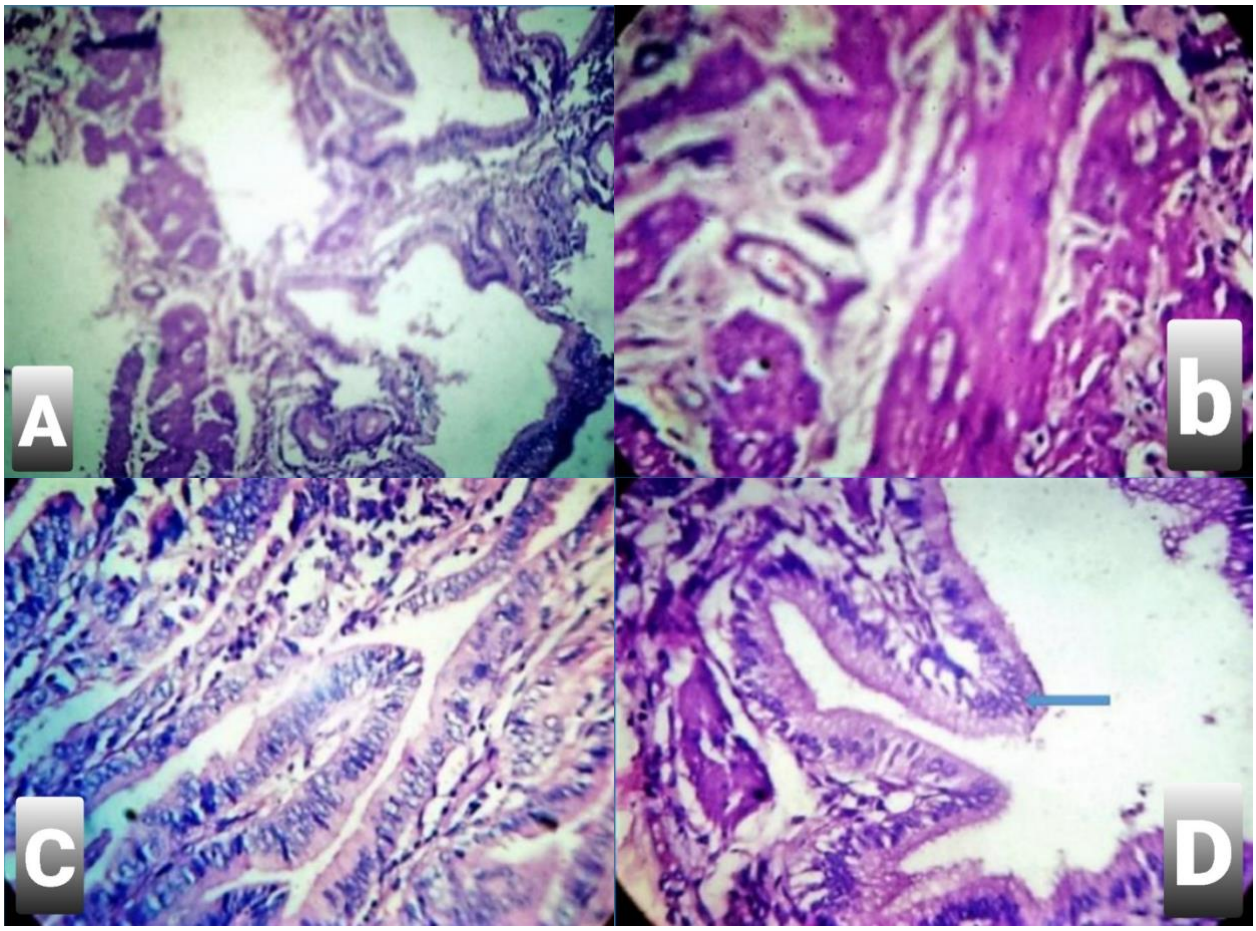

Fig.4 (A): Hyperplasia, H-Ex10 (Hyperchromatic Accentuated Folds).

(B): Muscle Hypertrophy, H-Ex40.

(C): Intestinal Metaplasia, H-Ex40 (Presence of Goblet Cells in Epithelium).

(D): Dysplasia, H-Ex40 (Disordered Intraepithelial Proliferation, that is Nuclear Stratification with Disorganisation).

5- Carcinoma.

The incidence of gallbladder neoplasms appears to vary according to geographical area, the incidence of cholelithiasis among the populations. has been an increase in East Europe and South America, and decrease in South-East Asia, Great Britain and Spain.The preoperative detection of gallbladder carcinoma represents a diagnostic challenge and largely determines the therapeutic management [8] . The gallbladder neoplasia associated with several risk factors, such as obesity, multiparity, and chronic *Salmonella*

typhi and *Helicobacter pylori* infection. However, the highest relative risk was associated with a cholelithiasis [10]. The cholecystectomy alone done in early cases while the cholecystectomy plus lymphadenectomy (or more radical hepatic resection) in advanced cases [8] . In the study of Oguzhan Dincel, Mustafa Goksu, Hamit Sinan Hatipoglu, etal. Gallbladder cancer was identified in five patients, with a prevalence of 0.4% in this sample. The range of patients age was 47-83 years. The result of p-value was 0.005 [6].
In the study of Amandeep Singh, Guramritpal Singh, and Deepika Sharma, etal. Gallbladder cancer was identified in two patients, with a prevalence of 2.0% in this sample. The range of patients age was 40-49 years. The result of p-value was 0.05 [4]. In the study that was done by Ana Karolina Gama Holanda, Zailton Bezerra Lima Júnior ,etal. Gallbladder cancer was identified in six patients, with a prevalence of 0.5% in this sample. The range of patients age was 26-60 years. The result of p-value was 0.013 [10]. In my opinion the higher occurrence in cancer related to age, the elderly age was most commen infectied and association of the tumor with gallbladder wall thickness. In the study of Ana groups and Oguzhan Dincel groups there was a significant association between the presence of cancer and age ≥ 60 years and wall thickness ≥ 0.3cm.

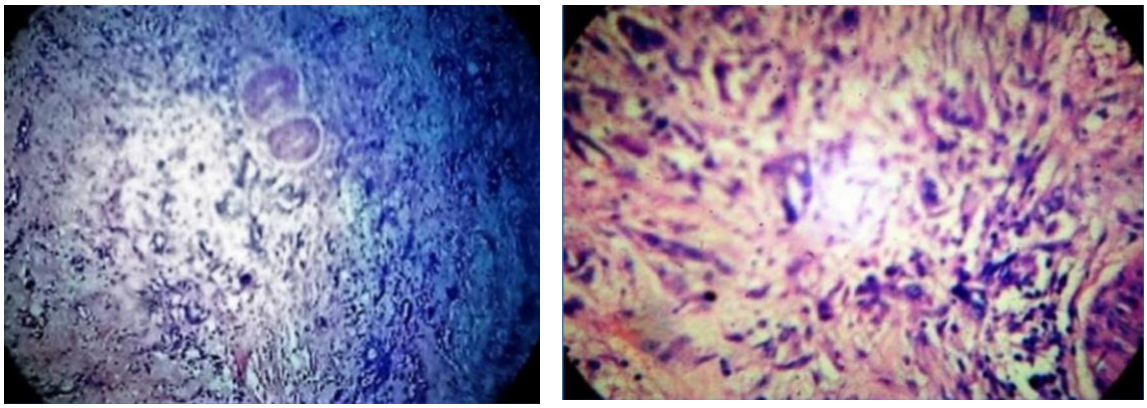

Fig.5(A): Adenocarcinoma, H-Ex10 (Well-Formed Glands with Nuclear Atypia in Desmoplastic Stroma). (B): Adenocarcinoma, H-Ex40.

Conclusion

1- The histopathological examination of gallbladder specimens is important to diagnose premalignant lesion. The histopathological examination of gallbladder specimens is an important step toward the confirmation of clinical and radiological diagnosis .

2- The most common cause of chronic cholecytitis is gallstones.

3- The most common finding associated with chronic cholecytitis is cholesterosis, Adenomatous hyperplasia, Xanthogranulomatous cholecytitis.

4- The most common pre malignant lesion found incidentally is metaplasia and Dysplasia.

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