Original Article

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A Study of Histopathological Changes in Gallbladder Mucosa in Patients with Cholelithiasis

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Abstract

Chronic cholecystitis is the most frequent inflammatory disease of gallbladder. Cholelithiasis produces diverse histopathological changes in gallbladder mucosa namely acute and chronic inflammation, glandular hyperplasia, granulomatous inflammation, cholesterosis, dysplasia and carcinoma. The variable appearance of gallbladder in chronic cholecystitis is reflection of differences in the degree of inflammation and fibrosis. This study was aimed to study the frequency and pattern of histopathological alteration in gallbladder mucosa in cholelithiasis in surgically resected specimens. The correlation between duration and severity of disease based on pathological changes was also assessed in order to elucidate the importance of early cholecystectomy. The study was conducted on 100 cases of chronic cholecystitis. The age of the patients ranged from 20 to 78 years with peak incidence 47.65% above third decade. Inflammatory mononuclear infiltrate was present in all 100 cases. The infiltrate was mild in 43% cases, moderate in 40% cases and severe in 17% cases. Fibrosis was mild in 38%, moderate in 18% and severe in 10% cases. Gallbladder malignancy was seen in 4 cases, with 1 case of mild dysplasia and 3 cases of severe dysplasia. The conclusion of the study suggest that grading of chronic cholecystitis should be used in routine reporting of gallbladder specimens so as to give complete information to surgeon.

Keywords: Cholethiasis; Carcinoma Gallbladder; Dysplasia.

Introduction

Cholelithiasis is derived from the greek root word: Chol means Bile, Lith means stone, iasis means process. Cholelithiasis belongs to civilization diseases as cholesterol stones have been noted in Egyptian Mummies that might have existed for more than 35 centuries. Nearly 10-15% of white adults in developed countries harbour gallstones, and world wide gallstone disease is increasing [1]. Chronic cholecystitis is the most frequent inflammatory disease of gallbladder. The highest prevalence of gall stones is noted in Native American Indians (prima) in Arizona with a frequency of 73% around age of 30 years. In Kashmir the prevalence of cholelithiasis is 6.12%. The same increases progressively to reach peak in 6th decade (Khuroo et al.) [2]. Although cholelithiasis is found most commonly in older individuals, yet in recent years an increase in incidence of a symptomatic cholelithiasis has been observed in children and young adults. Cholelithiasis produces diverse histopathological changes in gallbladder mucosa namely acute and chronic inflammation, glandular hyperplasia, granulomatous inflammation, cholesterosis, dysplasia and carcinoma. The variable appearance of gallbladder in chronic cholecystitis is reflection of differences in the degree of inflammation and fibrosis. The gallbladder may be shrunken or distended. The gallbladder wall is usually thickened, but it may be thin. The epithelium may be relatively normal, atrophic or hyperplastic

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with metaplastic changes. Mucosa of chronically inflamed gallbladder shows varying degrees of mononuclear infiltration and fibrosis. The diagnosis of chronic cholecystitis is based on demonstration of any of the following microscopic features: (1) a predominately mononuclear infiltrate, (2) fibrosis (3) metaplastic changes and dysplasia (Jessuram J) (3). There is a definite correlation between the duration and severity of gallbladder stone disease with pathological alteration in mucosa. A long duration stone produces necessary time for such chronic trauma to the mucosa and initiate sequence of pathological changes leading to dysplasia and carcinoma of gallbladder. The cause is due to gall stone induced chronic irritation and local production of carcinogens like secondary bile acids leading to dysplasia and cancer. A stone greater than 2-3 cm in diameter is associated with greater frequency of cancer provided there is long duration of stay in gallbladder.

This study was aimed to study the frequency and pattern of histopathological alteration in gallbladder mucosa in cholelithiasis in surgically removed specimens. The study was also designed to study the correlation between duration and severity of disease based on pathological changes in order to assess the importance of early cholecystectomy in patients diagnosed as cholelithiasis.

Methodology

The study was conducted in the Post-Graduate department of Surgery, Acharya SHRI Chander College of Medical Sciences and Hospital, Sidhra J&K, over a period of one year from November 2013 to October 2014. 100 patients fulfilling the eligibility criteria were enrolled in the study after taking informed consent. All the patients with cholelithiasis irrespective of the age were included in the study, however patients with acute cholecystitis, documented gallbladder malignancies, with co-morbidity like diabetes, thyroid disorders, hyperlipidemia, fatty liver and patients with cirrhosis were excluded from the study. Detailed history about duration of symptoms, age, sex, occupation, family and drugs was recorded. Thorough general, physical and systemic examination was done. Patients were subjected to various laboratory tests like complete blood counts, coagulation profile, serum urea and creatinine, blood sugar, serum electrolytes, serum bilirubin, SGOT, SGPT, alkaline phosphate, x-ray chest and ultrasound abdomen. Each case was analysed with respect to the following features: age, sex, duration of disease, ultrasound abdomen, gross features of gallbladder (wall thickness, appearance of mucosa, histopathological changes) and grading of severity. The gallbladder specimens were fixed in 10% buffered formalin and after proper labelling were sent to department of pathology for detailed gross as well as microscopic examination. Three blocks were prepared from each specimen so as to include the tissue from fundus, body and neck of gallbladder. At times extra blocks were taken from lymph nodes and other representative areas. Formalin fixed tissue was dehydrated with ascending grades of alcohol, cleared in xylene and finally embedded in paraffin sections. Three to five micron thick paraffin sections were cut on microtome, dewaxed and stained routinely with Haematoxyline and Eosin staining. Following histopathological changes like chronic inflammation, fibrosis, metaplasia and dysplasia were seen in the specimen of gallbladder. Severity of the chronic changes were graded and recorded. Chronic inflammation was graded as; (a) mild: not more than 10 lymphoplasmocytic inflammatory cells/hpf, (b) moderate: 11-30 lymphoplasmocytic inflammatory cells/hpf, (c) severe: more than 30 lymphoplasmocytic inflammatory cells/hpf. Fibrosis was graded as; (a)mild: uneven collagen deposition in less than 20% of the material, (b) uneven collagen deposition in 20% to 70% of the material, (c) severe: uneven collagen deposition greater than 70% of the material. Metaplasia was described as intestinal or pyloric type while as dysplasia was graded as, (a) mild: lower 1/3 dysplasia of epithelium above basement membrane, (b) moderate: when 1/3 to 2/3 of epithelium shows dysplasia, (c) severe: more than 2/3 of epithelium shows dysplasia.

Results

This study presents the data on 100 cases of chronic cholecystitis. The age of the patients ranged from 20 to 78 years with peak incidence 47.65% above third decade. The mean age in study was 41.85 years with male to female ratio 1:1.4. The spectrum of histopathological changes was found to be more prominent in females as compared to males with all histological changes mostly in females. In our study frequency of histopathological patterns and correlation between duration of pain and severity of disease is depicted in Table 1 and Table 2 respectively.

Table 1: Frequency of histopathological alteration in gallbladder mucosa

Diagnosis	Ch.inflammation	Fibrosis	Metaplasia	Dysplasia
Mild	43	38	0	1
Moderate	40	18	0	0
Severe	17	10	0	3
positive	0	0	11	0

Table 2: Correlation of duration of pain with severity of disease

Diagnosis	Mean± SD (months)			
	Ch.Inflammation	Fibrosis	Metaplasia	Dysplasia
Mild	4.14±2.02	7.21± 2.0	0	10
Moderate	8.70±3.38	12.33±5.01	0	0
Severe	16.94±5.29	18.20±5.99	0	19.33±8.08
positive	0	0	15.27±6.63	0
F-value	91.92	54.67	25.12	14.39

Discussion

Chronic cholecystitis is the most frequent inflammatory disease of the gallbladder. The variable appearance of gallbladder in chronioc cholecystitis is a reflection of the differences in the degree of inflammation, fibrosis metaplasia and dysplasia. Jaun Jose Barcia proposed a rational system for the microscopic observation and diagnosiss of the chronic inflammatory pathology of the gallbladder. A simple and reproducible scoring system of inflammation, fibrosis,metaplasia and dysplasia of gallbladder was proposed.we followed the system proposed by Barcia (2003) for our observations [4]. The observations and analysis of the present study provide a fair insight into the histopathologic patterns of chronic gallbladder disease.

The study was conducted on 100 cases of chronic cholecystitis.In this study the age of the patients ranged from 20 to 78 years with peak incidence 47.65% above third decade.Baidya R et al (2012) reported peak age in 5th decade [5]. The mean age in this study Was 41.85 years which is comparable to mean age of 38.9 years reported by Tyagi et al (1992). Male to female ratio was 1:1.4 in this study. The spectrum of changes in chronic inflammatory disease of gallbladder was noted and a rational system for the microscopic observation and diagnosis of the chronic inflammatory pathology was followed. In the present study inflammatory mononuclear infiltrate was present in all 100 cases. The infiltrate was mild in 43% cases, moderate in 40% cases and severe in 17% cases; whereas in the study conducted by Barcia (2003) it was mild in 28%, moderate in 57% and severe in 155 cases. Fibrosis was mild in 38%, moderate in 18% and severe in 10% cases; whereas in Barcia's study (2003) it was mild in 26%, moderate in 62%, and severe in 12% cases. Metaplasia was observed in 11% cases in this study whereas 75% specimen in Barcia's study (2003) had metaplasia.In this study of all cases of metaplasia 45.4% was of pyloric type and 54.5% was of intestinal type. Although the presence of metaplasia was associated with chronic changes,the extent of metaplasia did not correlate with the fibrosis or amount of inflammatory changes. So its production seems to be pathologically independent. Metaplasia is a strong supportive factor for the diagnosis of chronic cholecystitis. Gallbladder carcinoma is an extremely serious and frequently fatal lesion. Carcinoma of the gallbladder develops insidiously that its presence is not often suspected until the growth is well established. Gallbladder malignancy was seen in 4 cases in this study with 1 case of mild dysplasia and 3 cases of severe dysplasia as compared to 6.8% of cases as reported by Tyagi et al. (1992) [7]. Carcinoma of the gallbladder predominates in the females as was present in our study.Female to male ratio varies from 2:1 to 5:1 in various studies.In this study female to male ratio was 3:1 with peak incidence of gallbladder carcinoma above third decade in the age group of 51-60 years that comprised of 75% of cases of carcinoma.This is in accordance with Jessuram and Albores-Savedera [6] who reported maximum number of cases in the age group of 55-

75 years.In this study it is revealed that there is a strong correlation between duration of symptoms with severity of disease, as there is increase in progression of duration of symptoms,the severity of the histopathological changes increase significately. As is evident in patients with chronic inflammation, the patients with duration of symptoms less than 4 months severity of histopathological changes were mild.As duration progressed over and above one year,severity of histopathological changes increased from moderate to severe. Similar pattern of progression was noticed in both fibrosis and dysplasia Tyagi et al. [7]; hence making evident that early detection of gall stone disease requires early cholecystectomy, because of the progression of duration of symptoms increases severity of disease which ultimately can lead to severe complication like malignancy if left untreated.

Conclusion

This study was aimed at establishing the grades of chronic inflammation. The importance of establishing the grades of chronic inflammation is to give an idea to the surgeon about length of the disease alongwith severity; hence requiring early cholecystectomy in the benefit of the patient. The quantification of inflammatory changes in the gallbladder should be part of routine evaluation of the cholecystectomy specimens to give a rational, systemic and reproducible diagnosis of different pictures of the chronic inflammatory disease of gallbladder. This will result in most accurate diagnosis and uniform structured reported. Carcinoma was seen in 4% cases of chronic cholecystitis, so a meticulous search for its presence should be done in all gallbladder specimens of chronic cholecystitis. We concluded this study with the suggestion that grading of chronic cholecystitis should be used in routine reporting of gallbladder specimens so as to give complete information to the surgeon and patient.

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