Original Article

Pathology

Spectrum of Gall Bladder Diseases Diagnosed at Dow Diagnostic Reference and Research Laboratory, Dow University of Health Sciences

1. Saima Akram Butt 2. Tazeen Mustansar Raja 3. Naseem Ahmed Shaikh

1. Trainee, Dept. of Oral Pathology, Dr. Ishrat-ul-Ebad Institute of Oral Health Sciences, DUHS, Karachi
2. Asstt. Prof. of Pathology, DMC, DUHS, Karachi 3. Asstt. Prof. of Pathology, DMC, DUHS, Karachi

ABSTRACT

Background: Gallbladder is one of the most regularly encountered specimens in a pathology laboratory. A varied spectrum of diseases affects the biliary system that often shows similar clinical signs as well as symptoms. The objective of this study was to define the profile of gallbladder diseases in our area, and to establish potential correlations between different histopathologic features that were observed.

Study Design: Cross sectional study.

Place and Duration of Study: This study was conducted at the Department of histopathology In the Dow Diagnostic Reference and Research laboratory (DDRRL) from January 2011 to December 2011.

Materials and Methods: All cholecystectomies processed in Department of histopathology In the Dow Diagnostic Reference and Research laboratory (DDRRL), were reviewed. The data obtained were subjected to descriptive statistical analysis using SPSS version 16.0.

Results: Out of the total 824 patients, 684 patients were women (83%), whereas 140 (17%) were men, hence a female preponderance of the gall bladder diseases is seen. The mean age of the patients was 42.49±13.14 with an age range of 7-87. The bulk of these GBs were removed for symptoms related to chronic cholecystitis and cholelithiasis. Fourteen patients had primary gall bladder cancer (1.6%) whereas 810 patients were detected as having benign forms of gall bladder diseases.

Conclusion: Diseases of the gall bladder, time and again present with similar clinical signs as well as symptoms and a surgical pathologist should be very vigilant especially of precancerous lesions. With our study, we also concluded that elderly females with a longstanding history of gallstone disease should go through elective surgery even if there are no symptoms present.

Key Words: Cholelithiasis, Cholecystectomy, Gallbladder diseases

INTRODUCTION

The gallbladder is one of the most regularly encountered specimens in a histopathology laboratory.[1] Although often underappreciated, the gallbladder may be involved by a number of different pathological processes that have specific clinical correlates.[2] A vast range of diseases have an effect on the biliary system that often presents with alike clinical symptoms and signs.[1] The spectrum of gall bladder diseases range from the inflammatory disorders like cholecystitis and cholelithiasis to precancerous conditions like dysplasia, metaplasia and adenomas to full blown cancers including papillary and adeno-carcinomas. Gallstones are the most common pathology encountered in the biliary system. Interest in the formation and clinical management of gallstone disease date back to ancient times, as archaeological evidence suggest that members of the royal Egyptian family were affected with this disorder[3]. Although cancers are a rare finding in this organ, a surgical pathologist should especially be alert of precancerous lesions while processing and evaluating the specimen[1].

MATERIALS AND METHODS

A retrospective study of 824 cholycystectomies was conducted between January 2011 to December 2011, based on the histopathological reports with the purpose of identifying patients with gall bladder diseases. The histopathological reports were retrieved from the files of Pathology laboratory at Dow Diagnostic Reference and Research laboratory (DDRRL). The study data was collected by a single observer. The inclusion criteria involved histological confirmation of the gall bladder diseases. The criterion for exclusion was the absence of information concerning any of the studied variables. The following gross and histological features were detected: thickness of the gallbladder wall, inflammation, cholesterolosis, metaplastic (antral and intestinal) and dysplastic changes and cancers. The data obtained were subjected to descriptive statistical analysis using SPSS version 16.0.

RESULTS

Out of the total 824 patients, 684 patients were women (83%), whereas 140 (17%) were men; hence a female preponderance of the gall bladder diseases is seen (figure 1). The mean age of the patients was

42.49±13.14 with an age range of 7-87 years. The majority of these gall bladders were taken out for symptoms related to chronic cholecystitis and cholelithiasis. Fourteen patients had primary gall bladder cancer (1.6%) whereas 810 patients were diagnosed as having benign form of gall bladder diseases. The incidence of cholelithiasis, different forms of gall bladder inflammation, cholesterolosis, polypoidal lesions, and some precancerous lesions such as adenomas, antral and intestinal types of metaplasia and dysplasia in 824 patients are reported in Table I.

Table No.1: Pathological features of the gallbladder cases

Diagnosis	Female (n=684)	Male (n=140)	Total (n=824)
Thickness of GB wall			
1-2mm	250	28	278
>2mm	434	112	546
Chronic cholecystitis with Cholelithiasis	195	40	235
Type of inflammation			
Acute	6	3	9
Chronic	287	43	330
Acute on chronic	102	36	138
Eosinophilic	6	0	6
Xanthogranulomatous	7	2	9
Follicular	7	0	7
Cholestrolosis	46	8	54
Metaplasia			
Intestinal	6	4	10
Antral	3	1	4
Adenoma	1	1	2
Dysplasia			
Low grade	3	1	4
High grade	2	0	2
Carcinoma			
Papillary	7	0	7
Adenocarcinoma	6	1	7
Total	684	140	824

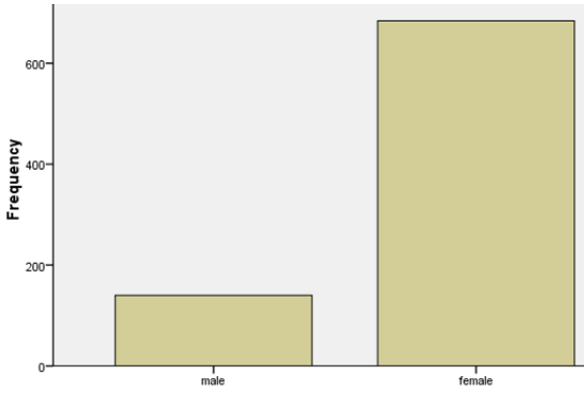

Figure No.1: gender distribution in all gall bladder diseases

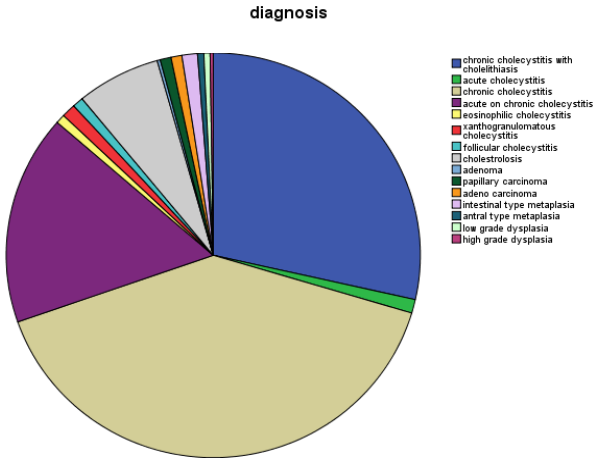

Figure No.2: frequency of different diseases encountered in gall bladder diseases

The incidence of cholelithiasis in our series was 28.5% (235patients). Of these, eighty three percent of patients were females and seventeen percent were males. Different types of inflammatory reactions were observed. Of these chronic type prevailed the most(40%). This was followed by patients with cholelithiasis (28.5%). Acute on chronic type of inflammatory reaction was observed in 138 patients (16.7%). Only two cases of adenoma were noted. Intestinal and antral type of metaplasia were both noted with a percentage of 0.01% and 0.004% respectively. 6 cases of metaplasia presented in this series.

DISCUSSION

The most common type of gall bladder disease encountered in our series was chronic cholecystitis alone followed closely by chronic cholecystitis with cholelithiasis. Many studies show a probable role of pregnancy[4], bacterial infections such as H.pylori[5] and iron deficiency anemia[6] in the formation of gallstones. Certain other studies also reveal that cholesterol stones have a higher frequency of occurring in urban populations having a western diet of style that has a higher proportion of refined sugars, saturated fats and proteins, whereas the pigment stones have a higher probability of occurrence in rural populations who eat a more traditional diet that is high in fiber as well as carbohydrates but low in fat and protein.[7-10] Variants of cholecystitis that are of importance are xanthogranulomatous cholecystitis and eosinophilic cholecystitis.

Xanthogranulomatous cholecystitis (ceroid granuloma, cholecystic granuloma) occurs due to rupture of the Rokitansky–Aschoff sinuses together with extravasation of bile that stimulate a florid fibroblastic as well as a histiocytic reaction.[11] only nine cases of xanthogranulomatous inflammatory condition were observed in our series. Eosinophilic cholecystitis has a threefold likelihood to be acalculous than usual

cholecystitis, and may be seen as a manifestation of parasitic infection, eosinophilic gastroenteritis, or drug intake.[11]

Cholestrolosis is illustrated by mucosal villous hyperplasia and excessive buildup of cholesterol esters within the macrophages in gallbladder epithelium.[12] The frequency of cholestrolosis was found to be 0.06% in our series. Their frequency, however, tends to vary in different series. This may be due to them having a very thin and a fragile stalk that leads to its detachment and therefore it floating along the passage of the bile, when the specimen is being handled grossly. A thorough inspection of the wall of a calculous gallbladder may be difficult and the movement of the stones within the gallbladder may also destroy this stalk.[1] The calculi can cause a prolonged damage to the mucosa which causes desquamation as well as mucosal epithelial regeneration. This is accompanied by metaplasia especially intestinal metaplasia.[1] On an average 50% of the cases presenting with chronic form of cholecystitis, also show some form of metaplasia, of which the most common is the gastric type.[13]

The lesions of epithelial origin, involved in epithelial carcinogenesis are adenomas and dysplasia, both of them having a different type of carcinogenic model. It is suggested that the malignant transformation occurs either through the dysplasia-carcinoma sequence[14,15] or the adenoma-carcinoma sequence.[16] Adenomas are uncommon polypoidal lesions and they can be easily categorized in to papillary, tubular and tubulopapillary types. These usually arise in the background of a normal mucosa of the gallbladder.[11] Adenomas and carcinomas are both said to have a malignant potential based on a morphometric analysis.[16] In his study, Kozuka etal suggests that most of the carcinomas of gall bladder arise from an already existing adenoma.[17] However morphological data[14] and molecular findings[18] obtained from completely-mapped early carcinomas show that most of the carcinomas of gallbladder do not arise from the pre existing adenomas and therefore the adenoma-carcinoma sequence may play a minor role in gallbladder tumorigenesis.

Epithelial dysplasia is broadly considered and accepted as a precursor lesion to the carcinoma of gall bladder.[11,14,19] The incidence of dysplastic lesions in cholecystectomy specimens is by and large associated with the geographic location as well as racial difference of the patients under study. Therefore, the figures vary, ranging from about 5% in studies conducted in North America[20] to 13.5-13.6% in studies carried out in Chile and Mexico [20,21] [21] and 0.018% in a study conducted in Turkey.[1] In our study the relative frequency of dysplastic lesions was 0.72%. These lesions show a female preponderance with a male: female ratio of 1:3. Dysplastic lesions can be sub classified in to two types, low grade and high grade (carcinoma in situ) types. This classification is based on the occurrence of abnormally polarized nuclei and also the other prominent nuclear abnormalities in the latter.[22]

The two types of gall bladder carcinomas observed in our series were adenocarcinoma and papillary adenocarcinoma which constituted a very small percentage of all the gall bladder diseases(1.6%). 80% of gall bladder cancers are adenocarcinomas and generally occurs in the 6th and the 7th decade of life. It also shows a female poreponderance it is more prevalent in Native and Hispanic Americans.[11] it constitutes one of the deadliest forms of gastrointestinal carcinomas.[11,23] Papillary adenocarcinomas comprise about 4% of gallbladder carcinomas, and they tend to form a protruding rather than an infiltrative mass, and carry a more favourable prognosis compared to other types of gallbladder carcinoma. This is because the exophytic component is not invasive. Invasion, if present, is often restricted to superficial layers of the lamina propria.[11]

CONCLUSION

Diseases of the gall bladder, time and again present with similar clinical signs as well as symptoms and a surgical pathologist should be very vigilant especially of precancerous lesions. With our study, we also concluded that elderly females with a longstanding history of gallstone disease should go through elective surgery even if there are no symptoms present

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Address for Corresponding Author:
Dr. Saima Akram Butt
E-mail: saimaakram@gmail.com
Contact No. +92-3333403522
Ph: +92-21-34523738
Add: 189- F Block 2, P.E.C.H.S,
Karachi Pakistan.