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Original Article

Institutional experience in the histopathological characteristics and frequency of gallbladder lesions

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Abstract: Purpose: Our aim in this study is to retrospectively examine cases in which cholecystectomy was performed and to determine incidental cancer cases. Materials and methods: We retrospectively examined the pathology reports of 1841 patients who underwent surgeries in the general surgery clinic for the treatment of gallbladder diseases between March 2006 and May 2015 and whose gallbladder materials were examined after surgery. Age, gender, pathological diagnosis and presence of gallbladder stones were recorded. Results: The average age of the 1841 patients (male/female: 585/1256) evaluated in this study was 50.37 ± 18.81 years (range: 2-97 years). Surgery for gallbladder disease was most commonly performed in the age range of 50-60 years. Chronic cholecystitis was the most common histopathological diagnosis (92.0%), followed by acute cholecystitis (5.1%), non-neoplastic lesions (1.74%), preneoplastic lesions (0.76%), carcinomas (0.33%) and lymphomas (0.1%). One or more gallbladder stones were detected in 955 patients. Of these, 93.4% and 4.1% patients were diagnosed with chronic cholecystitis and acute cholecystitis, respectively. Conclusion: Histopathological examination of gallbladder materials is important for identifying incidental benign and malignant tumours.

Keywords: Cholecystectomy, gallbladder tumours, pathology

Introduction

Cholecystectomies for gallbladder diseases are the most commonly performed surgeries in daily practice in surgical clinics [1]. Thus, cholecystectomy materials play an important role in pathology laboratories. In the histopathological examination of cholecystectomy materials, chronic cholecystitis is most commonly observed. Gallbladder stones are frequently observed in these cases. Gallbladder stones may cause changes such as irritation in the epithelium. A small number of cases may involve benign or malignant tumour [2-4]. Gallbladder cancer is observed histopathologically in 0.6%-5% of cases after cholecystectomy [3, 4]. Because these cases present findings similar to those observed in cases of chronic cholecystitis, a distinctive diagnosis cannot be made before surgery. However, considering the risk of metastasis, histopathological recognition of gallbladder cancer is important.

This retrospective study aimed to evaluate the pathological diagnoses in cases in which cholecystectomy materials were examined between March 2006 and May 2015.

Materials and methods

The study included 1841 cases in which cholecystectomy materials were examined between March 2006 and May 2015 at Dicle University Faculty of Medicine, Pathology Department. Age, gender, year of surgery, diagnosis (chronic cholecystitis, acute cholecystitis, non-neoplastic lesions, preneoplastic lesions, neoplastic lesions, lymphomas) and presence of stones were recorded from the pathology reports. The cases were categorised on the basis of the year of surgery.

The size of the gallbladder, wall thickness, presence of stones, changes observed in mucosa and presence of lesions were recorded using macroscopic examination of cholecystectomy

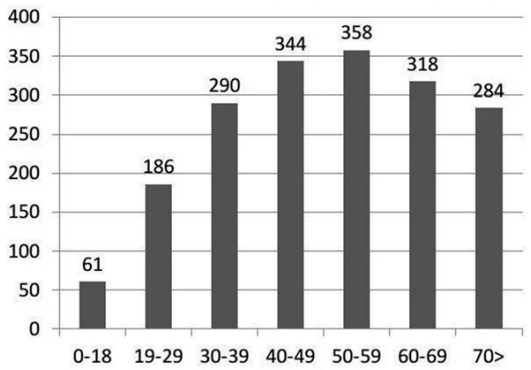

Figure 1. Age distribution of patients.

materials. One sample each was routinely taken from the gallbladder neck, body and fundus for examination. In patients suspected of having lesions, sampling was also performed in the suspicious areas. Haematoxylin and eosin-stained slides were examined using a light microscope.

Additional immunohistochemical staining was also performed when necessary. Cancer cases were classified according to the 2010 World health organization classification [5].

This study was conducted in accordance with the 2013 Helsinki Declaration and was approved by the ethics committee of our institution.

Data analyses were performed using Statistical Package for Social Sciences (SPSS Inc., Chicago, Illinois, USA) 15.0 package programme. The chi-square test was used to compare categorical data. A *P*-value of <0.05 was accepted as statistically significant.

Results

Pathology reports of 1841 patients were examined in this study. These included 1256 females and 585 males. The mean age was 50.33 ± 17.27 years for females and 49.91 ± 18.27 years for males. When examined according to the age range, cholecystectomy was most commonly performed in the age group of 50-60 years (**Figure 1**).

Chronic cholecystitis was the most common histopathological diagnosis (92.0%), followed by acute cholecystitis (5.1%), non-neoplastic lesions (1.74%), preneoplastic lesions (0.76%), carcinomas (0.33%) and lymphomas (0.1%) (**Table 1**). The diagnoses of the patients are given in **Table 1**. When the diagnoses were evaluated according to the age of the patients, it was observed that age was highest in carcinoma cases (65.33 ± 15.89 years) and lowest in polyp cases (40.23 ± 12.03 years). Only 1 patient diagnosed with carcinoma was under 50 years of age.

One or more gallbladder stones were detected in 955 patients. Of these, 93.4% and 4.1% patients were diagnosed with chronic cholecystitis and acute cholecystitis, respectively. Stones were observed significantly more frequently in women (697) than in men (258) ($P < 0.001$).

The yearly distribution of the cases is presented in **Figure 2**. Gallbladder materials constituted 1.7% of the total 106660 materials that were examined in our clinic between March 2006 and May 2015.

Discussion

Cholecystectomy is the most commonly performed surgery in routine practice. Distinctive diagnosis of malignant and benign gallbladder lesions before surgery is difficult. Thus, histopathological examination of all cholecystectomy materials is important.

Distinctive diagnosis of chronic or acute cholecystitis, metaplasia, dysplasia and benign or malignant lesions can also be made through histopathological examination. The aim of our study was to examine the histopathological diagnosis of cholecystectomy materials.

Gallbladder stones are among the most common diseases affecting the digestive system [6]. They are reported in 11%-36% of autopsies. The prevalence of gallbladder stones is associated with many factors such as age, gender and ethnic background. They are observed 3 times more frequently in women than in men, with an overall reported incidence of 51.9% for both men and women [6, 7].

Changes may take place in the epithelium when gallbladder stones are present. Irritation of the epithelium caused by gallbladder stones has been implicated in pathologies such as gastric metaplasia, dysplasia and gallbladder cancer

Table 1. The diagnoses of the patients

	n (%)	Age (years)	Gender (F/M)
Chronic cholecystitis	1693 (92.0)	50.02 ± 17.37	1175/518
Eosinophilic cholecystitis	7		4/3
Atrophic cholecystitis	2		1/1
Non-specific cholecystitis	1672		1161/511
Xanthogranulomatosis	12		9/3
Acute cholecystitis	93 (5.1)	54.81 ± 21.02	48/45
Carcinomas	6 (0.33)	64.33 ± 18.50	3/3
Adenocarcinoma	3		½
Squamous cell carcinoma	1		1/0
Carcinosarcoma	1		1/0
Signet ring cell carcinoma	1		0/1
Lymphoma	2 (0.1)	63.50 ± 13.43	0/2
Diffused large B-cell lymphoma	1		0/1
MALT	1		0/1
Non-neoplastic lesions	32 (1.74)	47.21 ± 14.94	
Polyp	13	40.23 ± 12.03	5/8
Adenomyomatosis	14	51.14 ± 16.98	11/3
Metaplasia	5		4/1
Preneoplastic lesions	14 (0.76)	79.22 ± 22.12	
Dysplasia	5	50.80 ± 15.25	3/2
Adenoma	9		6/3
Cyst hydatid	1		1/0

F: female, M: male, MALT: mucosa-associated lymphoid tissue.

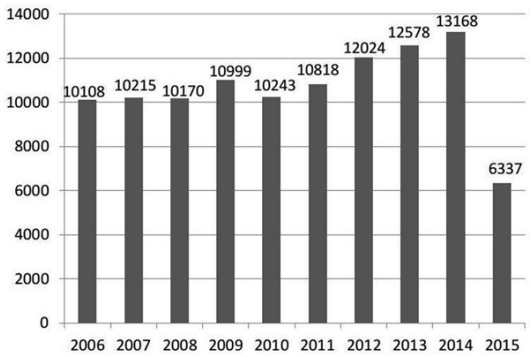

Figure 2. Total number of patients examined in pathologic clinics between March 2006 and May 2015.

[8, 9]. Metaplasia and dysplasia are known precursor of cancer lesions. Metaplasia frequency has been reported to be 0.72% in Turkey, 27.1% in Taiwan and 1.55% in England [10-12]. However, it was detected in only 0.3% of cases in our study. We believe that the low metaplasia frequency in our study, similar to the findings of the other study from Turkey, could be because gastric metaplasia is not reported since it is not accepted as a very important lesion, as indicated by Kesici et al. [13].

Benign tumours of the gallbladder are rare lesions. Their recognition is important because some have the potential to become malignant. Although there is no definite classification for benign tumours, polyps and adenomyomatosis were considered in our study. According to the literature, polyps are the most commonly observed benign tumours of the gallbladder [8, 14-16]. In line with these studies, polyps were the most commonly observed benign tumours in our study. These polypoid lesions present with symptoms similar to cholelithiasis. Adenomyomatosis is a common lesion; however, it has no malignant potential. Adenomyomatosis was observed in 14 cases in our study.

Because adenoma has the potential to turn malignant, its recognition is important. Kozuka et al. determined the malignant potential of adenoma in their study [17]. They reported that the malignant potential increases, particularly with an increase in the size of adenoma [18]. Adenoma was detected in 9 cases in our study. Gallbladder cancers are associated with poor prognosis and are observed in 1%-2% of cholecystectomy materials. In the literature 90% of patients diagnosed with gallbladder cancer were over 50 years of age, and gallbladder cancer was observed 2-4 times more frequently in females than in males. In our study, only 1 patient diagnosed with carcinoma was under 50 years of age. Carcinoma was observed with equal frequency in males and females in our study, which is in contrast with the results reported in the literature. Although the etiology of gallbladder cancer is unclear, 75%-90% of cases have been found to be related to gallbladder stones [17, 19]. Gallbladder stones

were present in only 20% of our cases. In the literature, 75% of cases have been reported to involve adenocarcinoma, whereas 5%-10% and 4%-7% involve adenosquamous carcinoma and mucinous carcinoma, respectively [20, 21]. In our study, adenocarcinoma was most commonly observed.

Apart from adenocarcinoma, carcinosarcoma and signet ring cell cancer, which are malignant tumours that are rarely observed in cases of gallbladder cancer, were observed in 1 case each. Carcinosarcoma is a malignancy with poor prognosis, constituting less than 1% of all gallbladder tumours. It includes both sarcomatous and carcinomatous components [22]. Signet ring cell cancer is rarely diagnosed in the gallbladder, with a limited number of cases being reported in the literature [23]. It is formed by cells containing intracytoplasmic mucin that pushes the nucleus towards the periphery and lateral spreading along the lamina propria can also be found. Extracellular mucin in varying amounts is usually present [24]. Tumour tissue formed by signet ring cells demonstrating a partial spreading pattern along the lamina propria as well as a partially diffused spreading pattern were observed in this study. These tumours contained approximately 20% extracellular mucin.

Gallbladder malignant lymphoma constitutes only 0.1-0.2% of all gallbladder tumours [25]. The origin of gallbladder lymphoma is controversial. Lymphoid tissue is not present in normal gallbladder mucosa [26]. It has been observed that most cases of gallbladder lymphoma are mucosa-associated lymphoid tissue (MALT) type or involve diffuse large B-cell lymphoma (DLBCL) [25-27]. In our study, MALT and DLBCL diagnoses were comparable to those reported in the literature.

The most important limitation of our study was its retrospective design and the fact that it does not provide information on the rates of premalignant lesions turning into malignant lesions.

In conclusion, histopathological examination of gallbladder materials is important for incidental tumour diagnosis. We believe that the results of this study are important for determining which diseases and rare lesions should be considered in the distinctive diagnosis of gallbladder lesions.

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Disclosure of conflict of interest

None.

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