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Original Article

Histopathologic features and frequency of gall bladder lesions in consecutive 540 cholecystectomies

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Abstract: The frequency of gall bladder lesions in cholecystectomies is not clear. The purpose of the present study is to report the morphologies and frequency of gall bladder diseases and lesions of 540 cholecystectomies in the last 10 years in our pathology laboratory. The age of patients ranged from 18 years to 93 years with a mean of 64.75 ±14.43 years. Male to female ratio was 213:327. Of these, 518 cases (96%) had gall stones. Eight (1.5%) were acute cholecystitis, 508 (94.1%) were chronic cholecystitis, 12 (2.2%) were adenocarcinomas, 1 (0.2%) was cystadenocarcinoma, and 11 (2.0%) were normal gall bladders. The frequency of histological lesions were as follows: acute gangrenous inflammation (8 cases, 1.5%), Rokitansky-Aschoff sinuses (RAS) (351 cases, 65%), microliths or inspissated bile in RAS (108 cases, 20%), adenomyomatous changes (16 cases, 3.0 %), focal abscess formations (12 cases, 2.2%), focal xanthogranulomatous changes (15 cases, 2.8%), mucosal ulcers (61 cases, 11.3%), cholesterosis (62 cases, 11%), cholesterol polyp (32 cases, 6%), pyloric gland metaplasia (292 cases, 54%), adenoma (7 cases, 1.3%), xanthogranulomatous cholecystitis (5 cases, 1%), invasive adenocarcinoma (12 cases, 2.2%), and cystadenocarcinoma (1 cases, 0.2%). In adenomyomatous changes, the epithelial proliferation was florid in a few cases, and no perineural invasions were seen. In pyloric gland metaplasia, no perineural invasions were recognized. All the 7 cases of adenoma were of intestinal type. In the 12 adenocarcinoma cases, one case arose in RAS without mucosal involvement, and 9 were tubular adenocarcinomas and 3 were papillary adenocarcinomas and 1 was mucinous adenocarcinoma. In the present series, there were no cases of heterotipc tissue, intestinal metaplasia, intraepithelial neoplasm, and other malignancies. These data may provide basic knowledge of the gall bladder pathologies.

Keywords: Gall bladder, incidence, histopathology

Introduction

Various lesions occur in the gall bladder [1, 2]. The most common is gall stones. Gall bladders with gall stones frequently show chronic cholecystitis. Chronic cholecystitis often shows muscular hypertrophy, lymphocytic infiltration, and fibrosis. Benign and malignant tumors also occur in the gall bladder. However, frequency of these lesions is not clear. The purpose of the present study is to report the morphologies and frequency of gall bladder diseases and lesions of 540 cholecystectomies in the last 10 years in our pathology laboratory.

Materials and methods

The authors retrospectively reviewed the HE preparation of cholecystectomies in the last 10 years in our pathology laboratory. Cutting of the gall bladder had been performed by the author. The cutting had been usual: a few specimens were cut from the cystic duct to gall bladder fundus in each case. When other lesions were found, they were prepared separately. The average number of preparations per case was 4-5. The sampling did not influence the pathological observations. Clinical records were also reviewed.

Results

A total of 540 cholecystectomies were found. The age of patients ranged from 18 years to 93 years with a mean of 64.75 ±14.43 years. Male to female ratio was 213:327. Of these, 518 cases (96%) had gall stones. The type of gall stones was not described in 213 clinical

Table 1. Disease and lesions of gall bladder among the 540 cholecystectomies

	Number	percentage
Diseases		
Normal	11	2%
Gall stone	518	96%
Acute cholecystitis	8	1.50%
Adenocarcinoma	12	2.20%
Cystadenocarcinoma	1	0.20%
Leions		
Acute gangrenous inflammation	8	1.50%
Rokitansky Aschoff sinus	351	65%
Micorilith in Rokitansky Aschoff sinus	108	20%
Adenomyomatous changes	16	3%
Abscess	12	2.20%
Focal xanthogranulomatous changes	15	2.80%
Ulcer	113	21%
Cholesterosis	62	11%
Cholesterol polyp	32	6%
Pyloric gland metaplasia	292	54%
Adenoma	7	1.30%
Xantogranulomatous cholecystitis	5	1%
Adenocarcinoma	12	2.20%
Cystadenocarcinoma	1	0.20%

records; the number and percentage of gall stones were cholesterols stones in 44 cases (19%), black or bilirubin stones 107 cases (47%), and mixed or combined stones in 75 cases (33%), and calcium carbonate stone in 1 case (1%). Detection of gall stones and gall bladder disease was made mostly by abdominal echo, and a few cases underwent endoscopic retrograde cholangiography. The reason for cholecystectomies was acute cholecystitis in 8 cases, gall stones with chronic cholecystitis in 475 cases, gall bladder polyps in 28 cases, suspected gall bladder carcinoma in 15 cases, and cholecystectomy of the normal gall bladder during gastric carcinoma in 11 cases.

Eight (1.5%) are acute cholecystitis, 508 (94.1 %) were chronic cholecystitis, 12 (2.2%) were adenocarcinomas, 1 (0.2%) was cystadenocarcinoma, and 11 (2.0%) were normal gall bladders (**Table 1**).

Acute cholecystitis was found in 8 (1.5 %) cases. They were characterized by phlegmonous neutrophilic infiltration with frequent ulcer formations, gangrenous changes, and abscess formations. One case showed acute perforation of the gall bladder.

Rokitansky-Aschoff sinuses (RAS) (**Figure 1**) were recognized in 351 cases (65%) with chronic cholecystitis. They were characterized by a cystic spaces lined by a layer of columnar epithelium in the fibromuscular or subserosal layers (**Figure 1**). Occasionally, the RAS epithelium showed marked proliferation. The presence of microliths or inspissated bile within RAS (**Figure 2**) was recognized in 108 cases (31 %) of the 351 cases. The microliths or inspissated bile was pigment ones in 56 cases and cholesterol ones in 52 cases. Foreign body reaction was present around the microliths or inspissated bile in 8 cases.

Adenomyomatous changes (**Figure 3**) were present in 16 cases (3.0%). They were characterized by many RAS and muscular hypertrophy. Epithelial proliferation was occasionally marked in the adenomyomatous changes. Pyloric gland metaplasia (**Figure 4**) was recognized in 292 cases (54%). It was characterized by the presence of glands resembling gastric pyloric glands, and mucin stains, which were performed in 5 cases, revealed neutral mucins. No perineural invasion was seen in both lesions. No intestinal metaplasia was recognized in the present series.

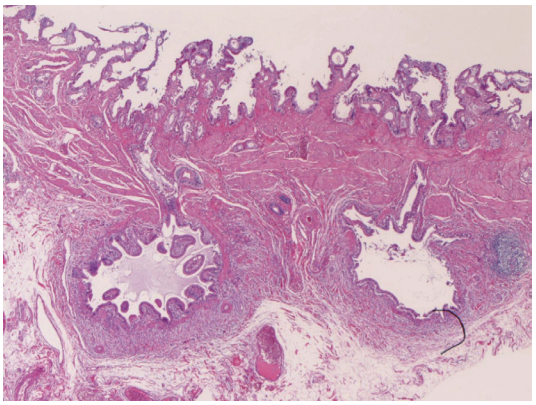

Figure 1. Histopathology of Rokitansky Aschoff sinuses. Two Rokitansky-Achoff sinuses are seen in the subserosa. HE, x40.

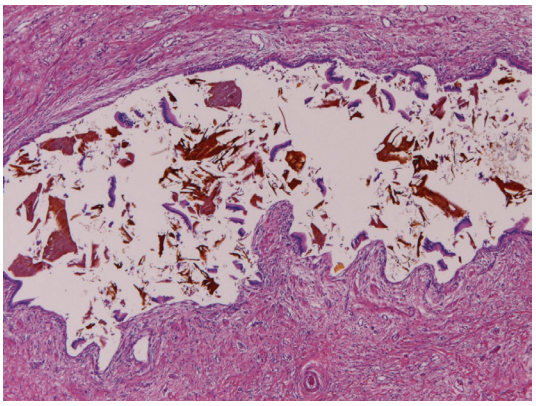

Figure 2. Histopathology of Microliths or inspissated bile within a Rokitansky-Aschoff sinus. They are pigment microliths. HE, x100.

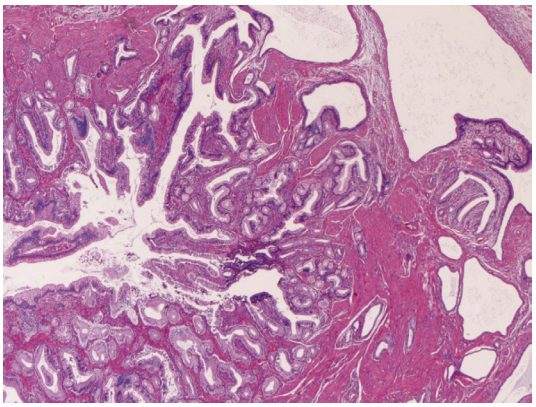

Figure 3. Histopathology of Adenomyomatous changes. Proliferation of cystic epithelium and hypertrophy of smooth muscles are evident. HE, x 40.

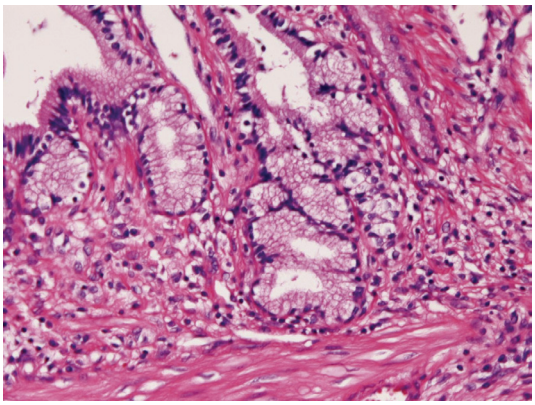

Figure 4. Histopathology of Pyloric glands metaplasia. Glands resembling gastric pyloric glands are seen. HE, x200.

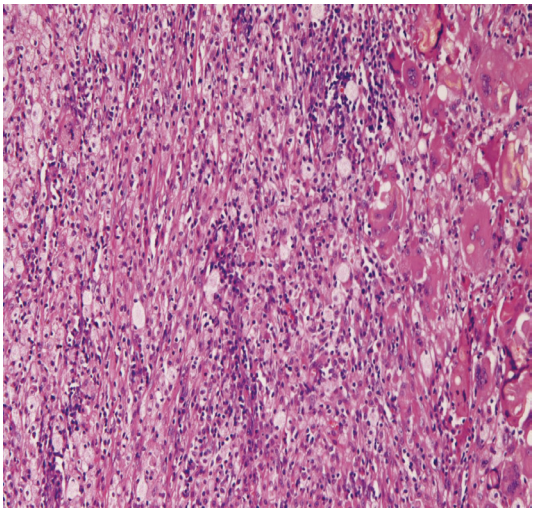

Figure 5. Histopathology of Xanthogranulomatous cholecystitis. Heavy infiltrations of macrophages, neutrophils and lymphocytes are seen. HE, x200.

Xanthogranulomatous cholecystitis (**Figure 5**) was noted in 5 cases (1%). The clinical diagnosis was carcinoma in 2 cases. It is characterized by diffuse infiltration of macrophages and other inflammatory cells. On macroscopic examination, this entity showed marked thickening of the whole gall bladder, and resembled gall bladder carcinoma. Focal xanthogranulomatous changes were noted in 15 cases (2.8%). Mucosal ulcers were recognized in 113 cases (21%). The focal xanthogranulomatous changes were frequently associated with mucosal ulcer formation. Focal abscess formations were noted in 12 cases (2.2%). They were character-

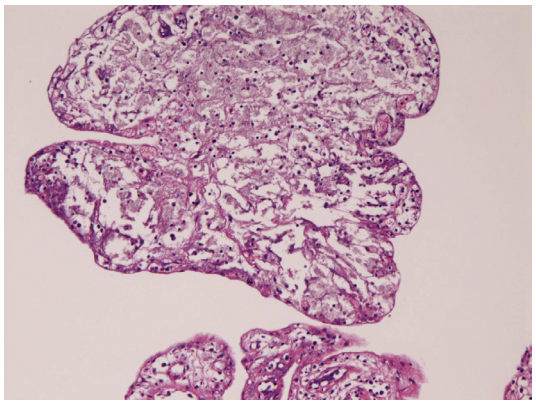

Figure 6. Histopathology of Cholesterol polyp. A polyp containing formy macrophages is seen. HE, x100.

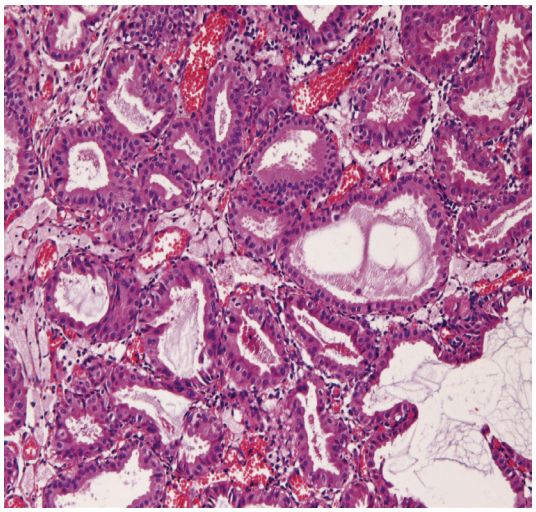

Figure 7. Histopathology of Tubular adenoma of intestinal type. A glandular adenomatous proliferation is recognized. HE, x100.

ized by islands of severe neutrophilic infiltrations.

Cholesterosis was identified in 62 cases (11%), and it was characterized by infiltration of formy macrophages in the mucosa. All cases of cholesterosis were associated with chronic cholecystitis. Cholesterol polyp (**Figure 6**) was seen in 32 cases (6%). It is characterized by a small polyp containing formy macrophages. It was frequently multiple, and grossly characterized by small yellow polyp.

Tubular adenoma (**Figure 7**) was demonstrated in 7 cases (1.3%). All of the adenoma was of intestinal type in this series. It is characterized by adenomatous proliferation of intestinal-type

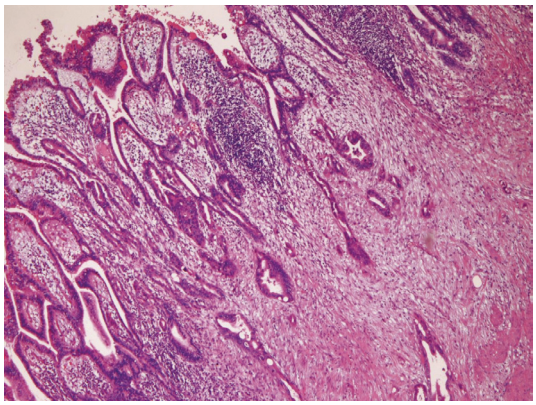

Figure 8. Histopathology of Gall bladder adenocarcinoma. Tubular adenocarcinoma with invasion is noted. HE, x40.

epithelium. Invasive adenocarcinoma (**Figure 8**) was recognized in 12 cases (2.2%). Of these, 8 were tubular adenocarcinomas and 3 were papillary adenocarcinomas and 1 was mucinous adenocarcinoma. One adenocarcinomas arose from RAS epithelium; the adenocarcinoma is not present in the mucosa but seen in the muscle or submucosa. There were gradual merge between carcinoma and RAS epithelium. This case was reported elsewhere [3]. In the other 11 cases、carcinomas were present in the mucosa; these cases are thought to arise from surface epithelium. Cystadenocarcinoma was noted in 1 case (0.2%). This case was reported elsewhere [4]. This was characterized by an invasive adenocarcinoma with cystic formations. No mesenchymal stroma was present in this case. Of these 13 carcinomas, 7 were incidental findings in pathologic examination. The cut margins were negative in all the 13 cases. The pathological stage was pT1a in 2 cases, pT1b in 6 cases, and pT2 in 5 cases. Follow-up study was not performed.

In the present series, there were no cases of heterotopic tissues, intestinal metaplasia, biliary intraepithelial neoplasm (BiliN) [5], and other malignancies.

Discussion

The histopathological features and incidence of gall bladder lesion varies depending on races, countries, and institutes. It is well known that gall bladder diseases affect more frequently women than men. The gall bladder disease most frequently occurs in middle age popula-

tion. The present series are compatible with these other data.

The frequency and pathologic features of acute cholecystitis is unclear. In the present series, acute cholecystitis was found in 1.5% of cases. They were characterized by phlegmonous neutrophilic infiltration with frequent ulcer formations, gangrenous changes, and abscess formations. One case showed acute perforation of the gall bladder.

The frequency of RAS is not known. RAS is though to be epithelial herniation due to increased gall bladder inner pressure. In general, RAS is rarely seen in normal gall bladders [2]. RAS is among the lesions of chronic cholecystitis [2]. In the present series, RAS were recognized in 65%. RAS epithelium occasionally showed marked proliferation. The frequency of microliths or inspissated bile within RAS was also unknown. In the present series, they were recognized in 31%. The microliths or inspissated bile was pigment ones in 56 cases and cholesterol ones in 52 cases. Foreign body reaction was present around the microliths in 8 cases. These findings suggest that the microliths or inspissated bile within RAS is frequent in chronic cholecystitis.

The frequency of adenomyomatous changes was unclear, but one Indian report showed that the incidence was 8.2% of 415 cholecystectomies [6]. In the present series, they were present in 3.0%. This difference may be due to the difference of the definition of adenomyomatous changes. Marked epithelial proliferation was occasionally recognized in the adenomyomatous changes in the present series. The incidence of pyloric gland metaplasia is unknown. In the present study, pyloric gland metaplasia was recognized in 54%. Albores-Saavedra et al. [7, 8] showed perineural invasion of adenomatous hyperplasia and pyloric glands metaplasia of the gall bladder. In the present study, perineural invasion was not seen in either lesion. No intestinal metaplasia was recognized in the present series. The authors think that the pyloric glands metaplasia emerges form gall bladder stem cells under chronic irritable inflammation.

The frequency of xanthogranulomatous cholecystitis is reported to be 8.9% according to Dixit et al. [9]. In the present series, it was noted in 1%. Focal xanthogranulomatous changes were recognized in 2.8%. Mucosal ulcers were recognized in 21 % in the present series Focal xanthogranulomatous changes were frequently associated with mucosal ulcer formation, suggesting that bile in the bladder walls incites the xanthogranulomatous changes. Focal abscess formations were noted in 2.2% in the present series.

The incidence of cholesterosis was reported to be 2.7 % in the Indian series [6]. In the present series, it was identified in 11%. This difference may be due to the difference in fat ingestion or accuracy of pathologic observation.

Cholesterol polyps and adenomas present with gall bladder polyps [10, 11]. The frequency of gall bladder polyp is reported to be about 4.5 % according to Jorgensen and Jensen [10]. In the present study, the frequency of cholesterol polyp was 6 %. It was frequently multiple, and grossly characterized by small yellow polyp.

Gall bladder tubular adenomas were classified into gastric type and intestinal type [1]. The frequency of tubular adenoma in the gall bladder was unknown. The present study revealed that the incidence of tubular adenoma is 1.3%. In the present series, all of the adenoma was of intestinal type.

In the present series, invasive adenocarcinoma was recognized in 12 cases (2.2%). Of these, 8 were tubular adenocarcinomas and 3 were papillary adenocarcinomas and 1 was mucinous adenocarcinoma. Two adenocarcinomas arose from RAS epithelium. Adenocarcinoma arising within RAS is extremely rare; only a few cases are reported in the literature [3, 12]. Cystadenocarcinoma was noted in 1 case (0.2%). This is also an extremely rare case; to the author's knowledge, only 5 cases are recorded in the English literature [4, 13-15]. This was characterized by an invasive adenocarcinoma with cystic formations. It is well known that hepatobiliary cystadenoma and cystadenocarcinoma is predominantly seen in middle-aged female and frequently have ovarian stroma-like mesenchymal stroma [13, 16, 17]. No mesenchymal stroma was present in the present case. Of these 13 carcinomas, 7 were incidental findings in pathologic examination.

In the present series, there were no cases of heterotopic tisues, intraepithelial neoplasms, and other malignancies.

The present data may provide basic knowledge of the gall bladder pathologies.

Conflict of interest statement

The author has no conflict of interest.

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