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MIMICKERS OF ADENOCARCINOMA GALLBLADDER

Arts

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ABSTRACT

Background: Aim of the study is to analyze many pathological mimickers of gall bladder carcinoma, which may be associated with over diagnosis or under diagnosis of the malignancy.

Materials & Methods: Retrospectively received 312 cholecystectomy specimens over a period of four months from January 2018 to April 2018.Surgical materials were received in the central histopathological laboratory in Government Medical College, Jammu. Majority of surgical cholecystectomies were done for cholelithiasis.

Results: Conclusion: Some of the benign conditions of gallbladder such as Rokitansky Ashoff Sinuses , Adenomyomatosis and Xanthogranulomatous cholecystitis may be misdiagnosed as adenocarcinoma and vice versa. It is possible to obtain accurate diagnosis by careful gross and histopathological examination.

KEYWORDS

Gall Bladder, Rokitansky Ashoff Sinuses, Adenomyomatosis, Xanthogranulomatous Cholecystitis

INTRODUCTION

One of the important frontiers of carcinoma is GIT malignancy, of which gall bladder carcinoma is of special mention [1].

In India, gall bladder carcinoma is the most common GIT carcinoma in north & central India[2,3] .Symptoms of gall bladder carcinoma often mimic those of chronic cholecystitis such as pain in the upper quadrant of abdomen,nausea,vomiting & features of obstructive jaundice [4].

Some benign conditions of gall bladder like Rokitansky- Ashoff sinuses, Xanthogranulomatous cholecystitis, Adenomyomatosis may mimic well-differentiated adenocarcinoma of gall bladder. This calls for meticulous histopathological examination. Latest studies have clearly mentioned & confirmed the role of histopathology in the diagnosis of gall bladder carcinoma & its mimickers.

MATERIALS & METHODS

We analysed 312 retrospectively received cases over a period of 4 months from January 2018 to April 2018, which included data retrieved from histopathological files of our department. The surgically resected cholecystectomy specimens were fixed in 10% neutral buffered formalin solution. All clinical data of the patients including age, gender & diagnosis were obtained from patients medical records. All the received surgical specimens were processed and then paraffin embedded blocks were prepared & were stained by routine Hematoxylin & Eosin stains & then examined microscopically. Excised gallbladder was opened along the longitudinal axis and the mucosa was examined macroscopically.

The gallbladder wall thickness of 1-2 mm was considered normal, wall thickness of 3 mm or more was considered thickened.

Gall bladder carcinomas were classified according to TNM system as proposed by American joint committee on cancer.

Inclusion criteria:

- Departmental cases sent after surgically resected cholecystectomy.

Exclusion criteria:

- Cases of common benign gall bladder disease with no histological diagnostic dilemma such as acute or chronic cholecystitis.
- Cases in which proper patient history record or tissue block could not be retrieved.

RESULTS:

Out of 312 cases, 246 were females & 66 were males. Patients were in the age group of 10-80 years.

Out of 246 females, in most of the cases cholecystectomy was done between 41 to 50 years and among males maximum cases were between the same age group.

It was found that out of 312 cases, five cases were of Well Differentiated Adenocarcinoma.

Out of 312 cases, 28 cases were showing deeply situated Rokitansky Ashoff Sinuses.

Adenomyomatosis was reported in three cases.

Eight cases were reported as Xanthogranulomatous Cholecystitis.

Table 1. Showing relevant microscopic diagnosis of mimickers of adenocarcinoma in cholecystectomy specimens included in study.

Moderately differentiated adenocarcinoma	5
Rokitansky Ashoff sinuses	28
Adenomyomatosis	3
Xanthogranulomatous cholecystitis	8

Table2: showing age wise distribution of cases included in the study.

Age group	No. of cases
1.0 – 19 yrs.	5
20 – 30 yrs.	49
31 – 40 yrs.	78
41 -50 yrs.	96
51 – 60 yrs.	47
61 – 70 yrs.	31
71 – 80 yrs.	6

Table3: Depicting gender wise distribution of cholecystectomy specimens.

Age	Females	Males
10 -19	3	2
20 -30	43	6
31 - 40	66	12
41 -50	76	20
51 -60	32	15
61 -70	22	9
71 -80	4	2

DISCUSSION:

Most Gall bladder carcinomas have no distinctive presenting features but often have symptoms resembling those of chronic cholecystitis[5] .Laboratory findings in Gall bladder carcinoma are also not diagnostic & may include hyperbilirubinemia, elevated serum CEA or CA 19- 9 [6] .Histopathological findings of gall bladder carcinoma sometimes create diagnostic dilemmas & sometimes gall bladder

carcinoma may give impression of benign gall bladder diseases such as RA sinus, Adenomyomatosis & vice versa [7].

Diagnosis of Gall bladder carcinoma has some potential pitfalls, which include under diagnosis of invasive well differentiated adenocarcinoma as deeply invasive RA sinuses, making an over diagnosis of gall bladder carcinoma when benign conditions such as RA sinuses ,adenomyomatosis of gallbladder ,Xanthogranulomatous cholecystitis are present.

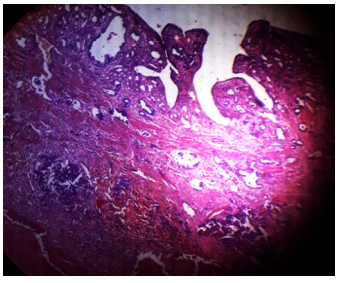

Figure1: photomicrograph showing adenocarcinoma gallbladder depicting diffuse desmoplastic reaction.

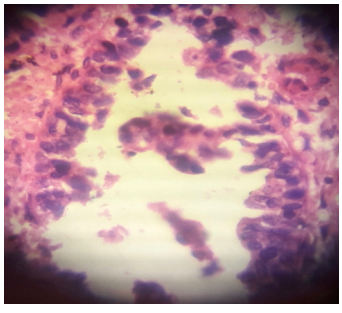

Figure 2

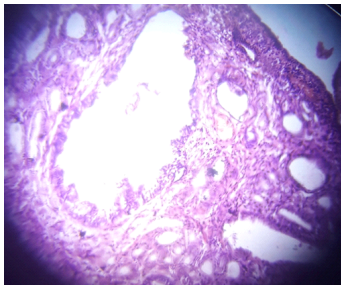

Figure 3:

Figure 2 and 3 : photomicrographs showing cytological atypia of glands in adenocarcinoma of gallbladder.

Well-differentiated adenocarcinoma can mimic RA sinus. RA sinuses can be present focally or throughout Gall bladder wall and some may extend into the muscular layer and perimuscular adipose tissue.

RA sinuses have connection to the surface epithelium and are continuous structures having a smooth contour. However Adeno carcinoma usually comprises of glands showing cytological atypia , Irregular and angulated contours and are arranged parallel to the surface . A prominent desmoplastic reaction usually favors Adenocarcinoma over RA sinuses. Other associated features of Adenocarcinoma glands are abnormal mitotic figures and intra glandular necrosis.

Giang et al reported cases of pitfalls in diagnosis of gallbladder carcinoma in which 2 cases were adenocarcinoma of gall bladder mimicking RA sinuses[7].

In one of the case they reported small glands embedded in bundles of smooth muscles , surrounding a deep vessel but resembling RA sinus , however the lining of deep glands presented cytological and subtle architectural atypia without significant inflammation and the surrounding stroma was more desmoplastic than inflammatory in nature . Final diagnosis was well-differentiated adenocarcinoma with associated surface dysplasia.

In another case they found dysplasia extending into deeply situated RA sinuses, mimicking invasion.

However lateral intramural growth was also present at one place without atypia-associated stroma, in which atypical small glands were closely juxtaposed to smooth muscle. Final diagnosis was well differentiated adenocarcinoma mimicking RA sinus with dysplasia.

Shirai et al differentiated RA sinus involvement by adenocarcinoma from stromal involvement by adenocarcinoma. The above study supported our observation that in case of dysplasia associated with RA sinus or when an adenocarcinoma progresses along RA sinus ,it is not surrounded by a desmoplastic stroma. However when malignant glands invade stroma they are surrounded by intense desmoplastic stromal reaction[8].

In our study we reported 28 cases of Rokitansky Ashoff sinuses which were deeply invasive and diligent microscopy revealed that mucosal invaginations were lined by epithelium which did not show any sort of atypia or desmoplastic stromal change.

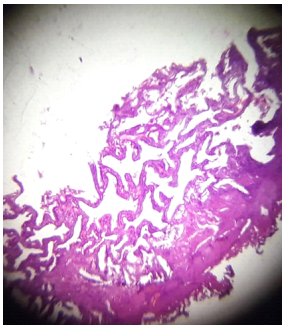

Figure 4: photomicrograph showing deeply located RA sinuses.

In Gallbladder Adenomyomatosis which is a benign condition characterized by proliferation of mucosal epithelium and hypertrophy of muscularis mucosae, with grossly formed mucosal invagination in hypertrophied muscularis, forming glands like spaces or branched ducts in muscularis mucosae [9] .In Adenomyomatosis there is thickening of gall Bladder in a diffuse pattern while localized thickness of Gall bladder is seen in adenomyoma [10] .Therefore adenomyomatosis presenting with thickened gallbladder wall , mucosal invagination into smooth muscle bundles and some times with perineural invasion may mimic gallbladder adenocarcinoma [9].

Varied names have been applied to this name in the literature, including adenomyomatosis , adenomyoma , diverticular disease, intramural diverticulosis, cholecystitis glandularis proliferans [11].

Dysplasia, carcinoma in situ and invasive carcinoma may arise from the epithelium of adenomyomatous hyperplasia. However most authors believe that the cause for development of carcinoma in adenomyomatous hyperplasia is the presence of stones, chronic inflammation and metastatic changes rather than adenomyomatous hyperplasia itself.

Albores Saavedra et al , reported nine cases of adenomyomatosis of gallbladder with perineural invasion mimicking adenocarcinoma of gallbladder [12].

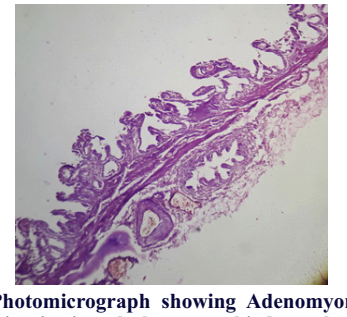

Figure 5: Photomicrograph showing Adenomyomatosis with mucosal invagination into the hypertrophied muscle.

In our study we reported 3 cases of adenomyomatosis with diffuse thickening of gall bladder wall and mucosal invagination into the

hypertrophied muscle with perineural invasion. Careful microscopy and deeper sections revealed single layer of tall columnar epithelial cells lined these invaginations and spaces were filled with bile and were reported as adenomyomatosis.

Xanthogranulomatous cholecystitis is a rare variant of chronic cholecystitis characterized by severe proliferative fibrosis with infiltration of macrophages and foamy cells within the gall bladder wall. This condition is benign in nature but often shows a destructive inflammatory process [13,14].

The inflammatory infiltrate and fibrosis cause the asymmetrical thickening of gall bladder wall and the formation of multiple yellowish brown nodules which often extend into the neighboring organs. The pathogenesis of Xanthogranulomatous cholecystitis is not fully understood till now, the presence of gall stones and biliary obstruction might play an important role, which causes the extravasation of the bile into the gallbladder wall via ruptured Rokitansky Ashoff sinuses and or ulcers of the surface mucosa [13,14].

Due to overlapping features between these two disease Xanthogra nulomatous cholecystitis is frequently misdiagnosed as Carcinoma Gallbladder[15,16].

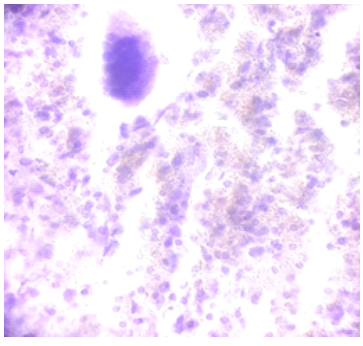

FIGURE 6: photomicrograph of Xanthogranulomatous change in the wall of gallbladder showing macrophages and foam cells along with a giant cell.

In a study conducted by Yi- Lei Deng et al 42 cases of Xanthogranulomatous cholecystitis were misdiagnosed as Gallbladder carcinoma either preoperatively or intraoperative but only 4 cases were corroborated pathologically. Indicating a high rate of misdiagnosis[17].

In our study we reported eight cases with definitive diagnosis of xanthogranulomatous cholecystitis there by indicating that definitive diagnosis has to be dependent on the histological examination.

It is therefore inferred that neither clinical manifestations and laboratory tests nor radiological methods provide a practical and effective standard in differential diagnosis between xanthogranul omatos cholecystitis and gallbladder carcinoma.

CONCLUSION

Accurate diagnosis is important for the proper surgical management of these patients. Despite several non invasive imaging and invasive techniques used to differentiate between mimickers of adenocar cinoma gall bladder, dilemma still exists and final diagnosis has to be dependent on the histological examination.

Although it is difficult to differentiate between benign mimickers and adenocarcinoma gallbladder it is possible to obtain an accurate diagnosis by careful intraoperative gross observation and histopathology is still the gold standard for diagnosis.

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