

Adenocarcinoma of Gall Bladder, Imitator in Clinical Manifestations, Radiological and Histopathological Findings

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Abstract Gall bladder adenocarcinoma is a rare malignancy with female predominance. Main patients are in the fifth to seventh decades. Clinical findings of gall bladder adenocarcinoma can be non-specific and the same as cholecystitis. The imaging is also non-specific with considerable overlap between benign and malignant lesions. Gall bladder adenocarcinoma may be overdiagnosed in histopathology by considering Rokitansky-Aschoff sinuses as malignant. It may be underdiagnosed in the cases of well-differentiated minimally invasive carcinoma. Incidental tumors are mainly in fundus and body of gall bladder. The first case was 80-year-old female with right upper quadrant pain, nausea and vomiting. Ultrasound was in favor of emphysematous cholecystitis. Postoperative diagnosis was acute gangrenous cholecystitis with tumor lesion suspicious for malignancy. Pathologist reported, moderately differentiated gall bladder adenocarcinoma extended to serosa in the neck of gall bladder. The second case was 58-year-old female with right upper quadrant severe pain, odynophagia, dysphagia, nausea and vomiting. Ultrasound examination showed gall bladder mass in the fundus and suggested gall bladder cancer. Pathologist reported, Poorly differentiated adenocarcinoma of gall bladder extended full wall thickness. Precise macroscopic evaluation is very important for finding of cases of gall bladder carcinoma even without clinical suspicion. For detection of malignancy, microscopic evaluation of all cholecystectomy samples is recommended. We suggest careful examination of cholecystectomy specimens especially in females more than forty with careful sampling of body and fundus.

Keywords: *gall bladder, adenocarcinoma, cholecystectomy*

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1. Introduction

Gall bladder adenocarcinoma is a rare malignancy [1]. Female to male ratio is in the range of 1.9-7 with mean age in the sixth decade. Main patients are in the fifth to seventh decades [2]. Clinically it may be misdiagnosed as chronic cholecystitis and discovered incidentally [1]. Incidental gall bladder adenocarcinoma is seen in 0.2-3% of cholecystectomies [1,3]. More than 89% of the gall bladder cancers are found incidentally [3]. Gall bladder adenocarcinoma may be overdiagnosed in histopathology by considering Rokitansky-Aschoff sinuses as malignant. It may be underdiagnosed in the cases of well-differentiated minimally invasive carcinoma [4]. The risk factors for gall bladder cancer are multiple gall stones, single large gall stone and gall bladder polyps [5]. Precise macroscopic evaluation is very important for

finding of cases of gall bladder carcinoma even without clinical suspicion [6]. For detection of malignancy, microscopic evaluation of all cholecystectomy samples is recommended [7]. Here we report two female patients of gall bladder adenocarcinoma with discussion on clinical symptoms, imaging findings and histopathology for better understanding the diagnostic pitfalls.

2. Case Presentation 1

An 80-year-old female was presented with right upper quadrant pain, nausea and vomiting since 3 days ago. In past medical history, diabetes mellitus, hyperlipidemia and ischemic heart disease were noted by the patient. Past surgical history was cataract surgery. Vital signs were stable. Physical examination was unremarkable except for right upper quadrant tenderness. Ultrasound examination was done at the admission. Liver had normal size and

parenchymal echo. Gall bladder had increased wall thickness and edema. Stone with maximum diameter of 17mm in gall bladder neck was mentioned. Luminal diameter was under 4cm containing biliary sludge and microlithiasis. Linear echogenous regions in gall bladder wall with artifact related to gas was in favor of emphysematous cholecystitis. No other significant finding was noted in ultrasound examination. Open cholecystectomy was done with preoperative diagnosis of emphysematous cholecystitis. Postoperative diagnosis was acute gangrenous cholecystitis with tumor lesion, suspicious for malignancy. Surgical specimen consisted of a perforated gall bladder measured 10x4cm. Cut sections revealed several stones measured up to 0.3cm. A gray area in the neck of gall bladder with diameter of 1.5cm was present. Mucosa was atrophic and wall thickness was 0.1cm. Pathologist reported: "moderately differentiated gall bladder adenocarcinoma extended to serosa (Figure 1). Tumor is located in the neck of gall bladder with diameter of 1.5cm. Surgical margin is involved by tumor. Vascular invasion is not present. Perineural invasion is present. Acute gangrenous cholecystitis with cholelithiasis is present." Written informed consent was obtained from the patient. No further follow up was available for the pathologist.

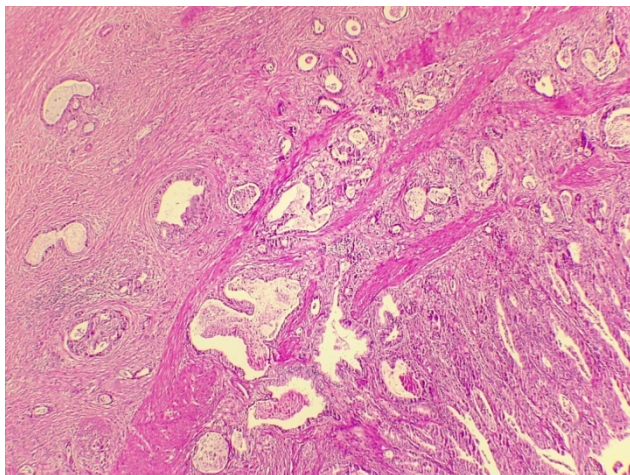


Figure 1. Moderately differentiated adenocarcinoma with atypical glands dissecting muscle fiber extending to serosa. Hematoxylin-Eosin staining x40 magnification

3. Case Presentation 2

A 58-year-old female was referred with right upper quadrant severe pain and odynophagia since last month. Dysphagia, nausea and vomiting were also present. In past medical history osteoarthritis and history of tubal ligation, 20 years ago was noted. Drug history consisted of calcium tablets. No history of cigarette smoking, alcohol or familial cancer was present. In general condition and physical examination malaise and weakness were present. Ultrasound examination showed gall bladder mass and suggested gall bladder cancer. Lymphadenopathy of hepatic hilum, celiac and head of pancreas with gastric outlet obstruction was noted. The patient underwent extended cholecystectomy surgery. Hepatectomy, partial lobectomy

(segment IV), cholecystectomy and gastrojejunostomy were done. The specimen consisted of gall bladder measured 10x4cm with gray firm mass measured 3cm in fundus (Figure 2). Stone measured 2cm. Wall thickness measured 0.3-2cm. Segment IV of liver was also resected. Pathologist reported: "Poorly differentiated adenocarcinoma of gall bladder, extended full wall thickness (Figure 3). Liver tissue is not involved by tumor. Tumor greatest diameter is 3cm. vascular invasion is present. Margin is free of tumor". Written informed consent was obtained for the report. No further follow up was available for the pathologist.

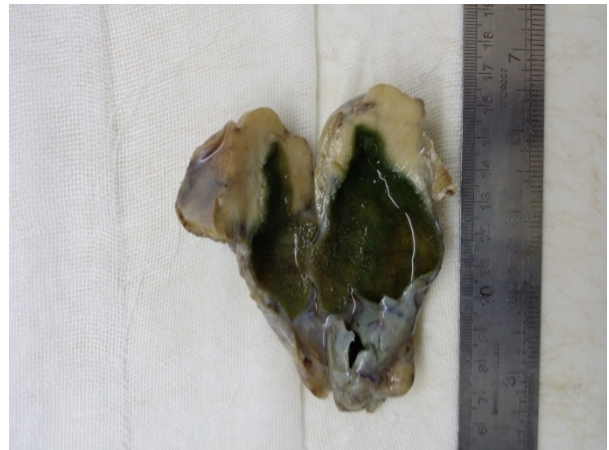


Figure 2. Gross appearance of tumor in the second case

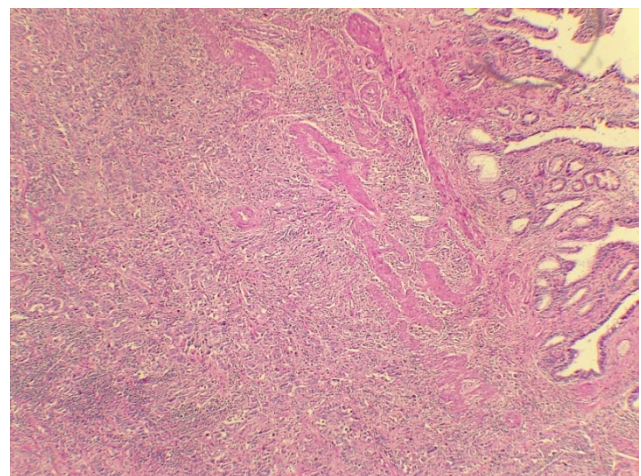


Figure 3. Poorly differentiated adenocarcinoma with infiltration of malignant cells extending to serosa. Hematoxylin-Eosin staining x40 magnification

4. Discussion

Clinical findings of gall bladder adenocarcinoma can be non-specific and the same as cholecystitis [1]. The imaging is also non-specific with considerable overlap with benign and inflammatory process [8]. In the study of Geramizadeh B et al [3] in Iran, 18 cases of incidental gall bladder adenocarcinoma were found that Male /Female ratio was 5/13. All patients had right upper quadrant pain in abdomen. Three patients had abdominal pain and jaundice. One had abdominal pain and anorexia, and

another one had abdominal pain with weight loss. Only six cases showed mild gall bladder wall thickening in ultrasound examination. Pathologist diagnosed all the cases as moderately differentiated adenocarcinoma. In the study of Waghmare RS and Kamat RN [9], seven cases (2.59%) of incidental carcinoma was found. Mean age was 50 years. Patients presented with pain, vomiting, and dysphagia. Similar to the previous study, six cases showed gall bladder wall thickening in ultrasound examination. All cases were moderately differentiated adenocarcinoma. All 6 cases of Jetley Sujata et al [8] had nausea, vomiting, RUQ pain and gall stone. None of them had mass and polyp in ultrasound examination. Even 5 cases had no evidence of malignancy at the time of surgery. Diffuse infiltration was seen in 68% of adenocarcinoma cases and the remaining with polyp hue [8]. Incidental tumors are mainly in fundus and body of gall bladder [2]. Morphology is tubular, papillary and mucinous adenocarcinoma in most of the cases [10]. Pathologist should consider differentiation, depth of invasion, amount of mucosal extension, perineural, lymphatic and vascular invasion along with lymph node metastasis in the report [2,9]. It is recommended that 3 levels examined for each paraffin block for evaluation of muscular invasion [8]. We suggest careful examination of cholecystectomy specimens especially in females more than forty with careful sampling of body and fundus according to above mentioned data.

5. Conclusion

Gall bladder adenocarcinoma is rare with diverse clinical manifestations, imaging and histopathology findings. It can imitate benign and inflammatory process. For detection of malignancy, microscopic evaluation of all cholecystectomy samples is recommended. We suggest careful examination of cholecystectomy specimens especially in females more than forty with careful sampling of body and fundus. Clinicians, radiologists and pathologists should consider this diagnosis in evaluating patients and gall bladder specimens.

Acknowledgments

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Conflict of Interest

The authors declare that there is no conflict of interest.

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