CASE REPORT

GALL BLADDER CARCINOMA - CLEAR CELL VARIANT IN CRIBRIFORM AND PAPILLARY PATTERN

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HOW TO CITE THIS ARTICLE:
Alba Thomas, D. Prem Charles, B. Krishnaswamy, P. Viswanathan, R. Baskaran. "Gall Bladder Carcinoma Clear Cell Variant in Cribriform and Papillary Pattern". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 15, April 14; Page: 3939-3944, DOI: 10.14260/jemds/2014/2380

ABSTRACT: Primary carcinoma of the gallbladder ranks as fifth most common malignancy of the gastrointestinal tract and adenocarcinoma accounts for 75% to 85% of cases. We are presenting a case of carcinoma gallbladder having clear cell pattern with cribriform pattern against the background of cholesterolosis of gall bladder.

KEYWORDS: Gallbladder adenocarcinoma, clear cell variant, cribriform pattern, cholesterolosis.

INTRODUCTION: Carcinoma of gall bladder is initially a silent disease. Patients present with tumors found incidentally at cholecystectomy for gall stones or with advanced symptomatology. A glycogen rich clear cell carcinoma is rarely seen. A choriocarcinomatous component in otherwise ordinary adenocarcinoma has been noted occasionally.¹ This is a disease of old age with peak incidence at 70 to 79 years of age and a female to male predilection of 3:1. Gallbladder carcinoma usually presents late in its course after tumor has already metastatized or spread locally. Most lesions have no distinctive presenting features but rather have symptoms that often resemble those of chronic cholecystitis.²

CASE REPORT: 35yr old male complained of abdominal pain for 8 days, which was confined to upper abdomen, aggravated on bending forward. There was history of constipation, and passage of grey colored stool. He had similar history one month back, which subsided on medication. He complained of icterus 2 months back for which ayurvedic medication was taken.

Examination revealed tenderness in right hypochondrium and in epigastrium with guarding of abdominal wall.

Routine investigations like blood test, liver function test, and renal function test were normal. Contrast CT Abdomen reported as hemangioma of liver with fundic polyp.

Patient had been taken for surgery. Laproscopic cholecystectomy attempted but converted to open cholecystectomy as there were local adhesions between stomach duodenum and omentum with inferior surface of liver, active bleeding was noticed from the hematoma already present at inferior border of liver. Hematoma evacuation was done. Gall bladder had been removed carefully by dissecting away from gallbladder bed and ligating carefully the cystic duct and artery.
Macroscopy: Partially cut opened Gallbladder measuring 7x4x2cm. Wall is of even thickness. Bile stained mucosa present. A growth 2.5x 1cm seen at distal end growing inward. In other container labeled liver tissue with blood clot measuring 2x.5cm. sections were taken and stained with haematoxylin and eosin stains.

Microscopic section studied from Gallbladder showed a malignant tumor composed of epithelial cells which tend to form papillary configuration. The epithelial cells showed clear cytoplasm and also exhibit cribriform pattern of growth; the cells in cribriform pattern of growth showed varying degrees of pleomorphism. Calcified spherules are present. There are extensive areas of hemorrhage and necrosis. Similar tumor cells are present in the tissue labeled liver.

FINAL DIAGNOSIS: Clear cell carcinoma of the gallbladder.

DISCUSSION: Pain is probably the most common presenting symptom, and other signs or symptoms include jaundice, a palpable right upper quadrant mass, and nausea, vomiting anorexia, jaundice and weight loss.  

Laboratory findings are also non-diagnostic and may include hyperbilirubinemia, elevated serum alkaline phosphatase level, and other markers of extrahepatic biliary tree obstruction and/or elevated serum carcinoembryonic antigen (CEA) or carbohydrate antigen 19-9 (CA19-9). The latter are nonspecific findings for malignancy as they may also be elevated in obstructive biliary disease or other types of adenocarcinoma.

Etiologic factors include inherent genetic predispositions as well as congenital anomalous arrangements of the pancreaticobiliary duct. Gallstones are found in more than 80% of patients with gallbladder carcinoma. Most consider chronic irritation of the stones as the promoter of neoplastic transformation. Diffuse calcification, or Porcelain gallbladder, is another condition that has high association with adenocarcinoma Chronic Salmonella typhi infection of gallbladder and exposure to chemicals like Methycholanthrene, O-aminoazotoluene, and Nitrosamines imposed increased risk for carcinoma. This patient didn’t had any of above risk factors.

Adenocarcinoma usually results in localized thickening of gallbladder wall after causing it to bulge into lumen. Less frequently, they may result in a diffuse thickening of the gallbladder wall or form an intraluminal papillary growth. Gallstones are present in vast majority of cases. Approximately 90% of the carcinomas arise in body or fundus of gallbladder, remainder occur in neck. Invasion into adjacent liver parenchyma may occur in as many as 70% of the cases.
Most common neoplasm is infiltrative adenocarcinoma, which is moderately well-differentiated to well-differentiated foci of tubular glands in about 40% to 50% cases. Up to 30% of cases may be poorly differentiated cancers, and 12% are papillary variant; 12% are mucinous cancers and 7% are adeno squamous or squamous variant.2

The more well differentiated tumor glands are lined by columnar to cuboidal tumor cells. Sheets or cords of tumor cells or single tumor cells may be present as well. The nuclei is usually round and oval and are often located basally or centrally. The cytoplasm may be eosinophilic, slightly granular, pale or clear, or mucinous. Occasional goblet, paneth or endocrine cells may be seen. The number of mitotic figures may vary.2

The papillary variant of adenocarcinoma is a well differentiated lesion that grows outward into the lumen of the gallbladder. The tumor cells proliferate on fibrovascular stalks. Such tumors may fill the lumen of gallbladder before invading the wall and so are often associated with a better prognosis than are the more common infiltrative types.2

Clear cell variant of carcinoma is composed of sheets, nests, trabeculae, glands, or small papillary structures consisting of tumor cells with clear cytoplasm. The cytoplasm is negative for acidic and neutral mucins and contain Periodic Acid Schiff positive material that get digested with amylase. With electron microscopy these cells are seen to contain glycogen, prominent rough endoplasmic reticulum, and a moderate number of mitochondria.2

Cribriform type is other type of adenocarcinoma. This type is composed primarily of groups of tumor cells with well -defined punched out spaces lined by fairly uniform tumor cells with hyperchromatic nuclei. The overall pattern mimics that of cribriform breast carcinoma, and possible metastases from a breast primary should be excluded when such a lesion is noted in gallbladder.2

Gall bladder has a great propensity to invade liver directly and to a lesser extend the stomach and duodenum ;it also metastasizes frequently to liver, cystic and pericholedochal lymph nodes in the lesser omentum and lymph nodes behind the first portion of the duodenum. The frequency of lymph node involvement is highly dependent on the depth of invasion of the primary tumor. Almost half of patients already have metastatic disease at the time of surgery. More distant sites often involved include mediastinal, bronchial or supraclavicular lymph nodes. Implants of the peritoneal surfaces can lead to intra-abdominal carcinomatosis and ascites and invasion into adjacent hollow organ can lead to biliary -enteric fistulas. One most serious complication is perforation of gall bladder which leads to peritonitis, abscess or fistula.Bilateral spread to the ovaries resulting in Krukenberg tumor may rarely be seen.3

Treatment of gallbladder carcinoma is primarily surgical, its extent depending on the stage of the disease. Nevin et al recommend cholecystectomy alone for stages 1 and 2, radical surgery for stages 3 and 4 and palliation alone for stage 5. It has been claimed that the addition of adjuvant chemotherapy or radiation therapy in patients treated surgically lengthens the survival time.3

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GROSS PICTURES:

![Gross Picture](image1)

**Fig. 1:** Gallbladder showing a growth of 2.5x1 cm from the distal end growing inward

MICROSCOPIC PICTURE:

![Microscopic Picture](image2)

**Fig. 2:** 4x: Papillary projections lined by dysplastic cells

**Fig. 3:** 10x: Papillary projections with fibrovascular core

![Microscopic Picture](image3)

**Fig. 4:** 10x: Blood clots containing poorly differentiated tumour cells

**Fig. 5:** 40x: Tumour cells showing high degree of dysplasia and anaplasia
Fig. 6: 10x: Cholesterosis with cholesterol clefts and giant cell reaction

Fig. 7: 40x: Lipid laden macrophages seen

Fig. 8: 10x: Papillary carcinoma of gall bladder with calcified spherules

Fig. 9: 40x: Papillary projection with fibrovascular core lined by tumor cells of high degree of dysplasia

Fig. 10: 10x: Cribriform pattern with bile deposits

Fig. 11: 40x: Clear cell with Papillary configuration
CASE REPORT

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Date of Submission: 20/02/2014.
Date of Peer Review: 21/02/2014.
Date of Acceptance: 12/03/2014.
Date of Publishing: 09/04/2014.

Fig. 12: 40x: Tangential cut of papillary configuration