

## ATYPICAL PRESENTATIONS OF GALL BLADDER CARCINOMA

T Karthik<sup>a</sup>, A V P Sivalingam<sup>a</sup>, Ramya Ramakrishnan<sup>a</sup>, Shalinee Rao<sup>b</sup>

### ABSTRACT:

Gallbladder carcinoma is a highly malignant and uncommon tumour that affects predominantly women in the 6<sup>th</sup> and 7<sup>th</sup> decade of life. Most of the patients are either asymptomatic or have only dyspeptic symptoms and usually present at an advanced stage, when treatment options becomes limited. Some patients may have atypical presentations and unusual associations.

In this case report, we document two cases of carcinoma gallbladder who presented with an acute abdomen. Relevant literature about atypical presentations of carcinoma gallbladder is also reviewed.

**Key Words:** acute abdomen, atypical presentation, carcinoma, gallbladder.

SRJM 2011;4:42-44

### INTRODUCTION:

The incidence of gallbladder carcinoma is 1.2 cases per 100,000/ year and increases with age, particularly after the sixth decade of life.<sup>[1]</sup> Ethnic background and geographical location are important factors in the incidence of this cancer. It is more common in Central and South America, Japan and North India. Risk factors include cholelithiasis, calcified gallbladder wall, adenomatous gallbladder polyps, choledochal cyst and anomalous pancreatobiliary junction.<sup>[2,3,4]</sup>

The clinical presentation of gallbladder cancer is identical to the more prevalent symptoms of biliary colic and/or chronic cholecystitis, making it difficult to suspect the diagnosis pre-operatively. Some patients are completely asymptomatic until widespread metastasis occurs.<sup>[5]</sup> Rarely, patients with gallbladder carcinoma may have atypical presentations and unusual associations. In this case report, we discuss the case details about two of our patients with carcinoma gallbladder one of which presented with features of emphysematous cholecystitis and another with acute pancreatitis.

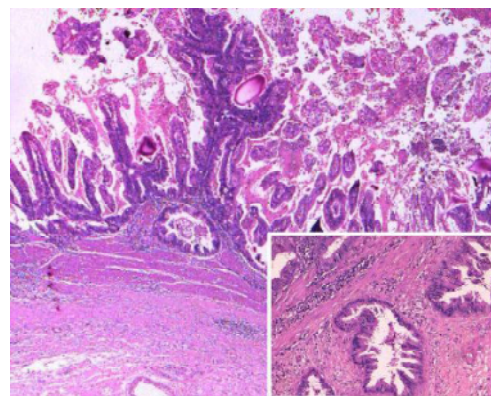
### CASE DETAILS

**Case 1:** A 45 year old female was brought to the emergency department with complaints of epigastric pain and vomiting for three days. On examination, she had mild tachycardia and normal blood pressure. She was icteric and afebrile. Abdominal examination revealed tenderness in the epigastrium with no features of peritonitis. Blood investigations revealed leucocytosis, mild obstructive jaundice with elevated pancreatic enzymes (Serum amylase- 431/l, Serum lipase- 1102/l). Ultrasonogram of the abdomen showed distended gallbladder filled with sludge and dilatation of the common bile duct. A diagnosis of



**Fig. 1:** Cut open gall bladder showing mucosa studded with glistening nodules

gallstone pancreatitis was made and the patient was managed conservatively. Subsequently, patient was taken up for open cholecystectomy after symptomatic improvement and reduction of serum pancreatic enzyme levels. Intra-operatively, the gallbladder was thick walled and distended. Cholecystectomy was done by the standard technique. On cutting open, the gallbladder was seen to be studded with polypoidal nodules over the entire mucosa. No gall stones were identified (Fig 1). Histopathology of the excised specimen revealed papillary adenocarcinoma of the gallbladder (Fig 2). Grossly the tumor was seen involving the fundus, body and portion of



**Fig. 2:** Tumour cells arranged in papillary pattern showing stratification and nuclear atypia (Hematoxylin and eosin X 10 x); Inset show islands of tumour cells arranged in glandular pattern infiltrating the muscle layer (Hematoxylin and eosin X 10)

### CORRESPONDING AUTHOR :

**Dr. RAMYA RAMAKRISHNAN**

Professor of General Surgery, SRMC & RI  
Sri Ramachandra University,  
Porur, Chennai-116.

e-mail : ramyadr99@yahoo.co.in

<sup>a</sup> Dept. of General Surgery, SRMC & RI

<sup>b</sup> Dept. of Pathology, SRMC & RI

the neck. One lymph node was identified in the specimen which was found to be positive. The tumor was moderately differentiated with a pathologic staging of p T<sub>2</sub> N<sub>1</sub> cM<sub>0</sub>. Patient was referred to medical oncology for further management.

**Case 2:** A 41 year old male, a smoker and alcoholic, visited the outpatient department with complaints of dyspepsia for one month and acute abdominal pain for three days. On examination, patient was febrile and had tenderness in the right hypochondrium and a positive Murphy's sign was elicited. Ultrasonogram of the abdomen revealed a distended gallbladder with pericholecystic fluid and specks of air in the wall of the gallbladder. The total leucocyte counts was elevated. His liver function tests, renal parameters and pancreatic enzymes were within normal limits. A diagnosis of emphysematous cholecystitis was made and patient was taken up for laparoscopic cholecystectomy. During surgery, gallbladder was found to be oedematous and the Calot's triangle could not clearly be identified. Hence, it was converted to an open surgery and gallbladder was removed and sent for histopathological examination. Grossly the gall bladder was thickened and mucosa flattened out. Sections showed mucosal ulceration with islands of atypical cells arranged in glandular pattern with surrounding desmoplastic stromal reaction (Fig 3). A histopathological diagnosis of moderately differentiated adenocarcinoma was made. Post-operative period was uneventful. Patient is under follow-up with medical oncology.

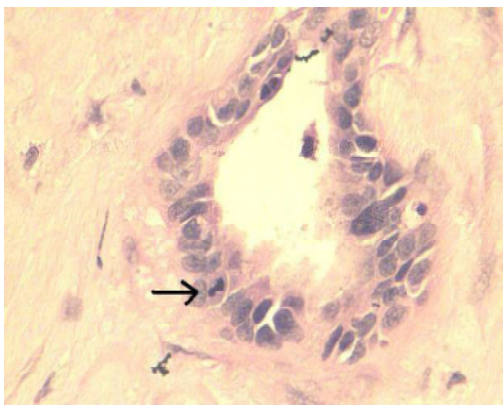


Figure 3: Atypical cells arranged in glandular pattern with surrounding desmoplastic stromal reaction, Note an atypical mitosis (arrow)(Hematoxylin and eosin X 40)

## DISCUSSION

Carcinoma of gall bladder is an uncommon malignancy with a high incidence in certain parts of the world. The incidence of gall bladder cancer in India is very high in the north as compared to the Southern India.<sup>[6]</sup> It is found incidentally in 1-2% of patients undergoing cholecystectomy for symptomatic cholelithiasis.<sup>[7]</sup> Early stage tumours(T1) do not require any further surgery. Exceptions to this rule are presence of intra-operative bile spillage and cystic duct

margin positivity. Unfortunately, most of the patients are asymptomatic and present in an advanced and unresectable stage requiring only palliative treatment.

The most common factor associated with gall bladder carcinoma in India is the presence of gall stones, while in Japan and Chile, it is the presence of anomalous pancreatic biliary duct junction (APBDJ).<sup>[8,9]</sup> Pathogenesis of carcinoma arising in APBDJ is different as compared to carcinoma from cholelithiasis. Constant irritation of epithelium of gall bladder from reflux of pancreatic juice and frequent K-ras mutation at codon 12 results in gall bladder carcinoma in APBDJ.<sup>[10,11]</sup> While the sequence of events in carcinoma occurring due to gall stone starts with inflammation of mucosa with subsequent metaplasia followed by dysplasia with p53 mutation ultimately transforming into a carcinoma.<sup>[12,13]</sup> Misra et al in a study documented over-expression of p53 protein in 70% of cases with gall bladder carcinoma that were associated with gall stones.<sup>[14]</sup>

Gall bladder carcinoma is usually diagnosed at an advanced stage. In most series, the 5 year survival rate is 3-5%<sup>[15]</sup> since they are usually asymptomatic and presents only at an advanced stage. Symptomatic patients have features of dyspepsia or biliary colic. Rarely, they may present with an acute abdomen. Occasionally, patients with gallbladder cancer may have atypical presentations and unusual associations. Haribakthi et al studied a large series of carcinoma gall bladder in a tertiary health care center of North India. Their study included 324 patients of which, 26(8%) had atypical clinical presentations and 34(10%) with unusual associations.<sup>[16]</sup> The atypical presentations included empyema, acute cholecystitis, post-cholecystectomy biliary stricture, carcinoma head of pancreas, gastric outlet obstruction and liver abscess. In our experience, we encountered two cases of carcinoma gallbladder one presenting as emphysematous cholecystitis and another with acute pancreatitis. In the former case, it would have probably occurred due to tumour blocking the cystic duct with distension and mucosal necrosis with secondary infection. While, in the latter case of acute pancreatitis, the mucoid material produced by the papillary carcinoma would have obstructed the pancreatobiliary junction resulting in pancreatitis. Anomalous pancreatic biliary duct junction is also known to cause pancreatitis by way of reflux of bile and pancreatic juice into the pancreas. This indicates that the patient who presented with acute pancreatitis could have had an anomalous pancreatobiliary junction. Another unusual feature about our patients was their age at presentation. Carcinoma of the gallbladder is unusual among patients less than sixty years of age and both our patients were less than fifty years of age. Rashid et al found a genetic abnormality involving extensive instability in repeated nucleotide sequences(microsatellites).<sup>[17]</sup> This condition is termed as microsatellite instability, and it occurs most often in patients with gallbladder cancer at a younger age.

To conclude, unusual presentations of gallbladder cancer in certain geographic locations (like India) must be thought of when managing patients with acute abdomen with symptoms related to the hepatobiliary/ pancreatic systems.

#### REFERENCES:

1. Lazcano-Ponce E C, Miquel J F, Munoz N, Herrero R, Ferricio C, Wistuba II, et al. Epidemiology and molecular pathology of gallbladder cancer. *CA Cancer J Clin.* 2001;51: 349-64.
2. Kondo S, Nimura Y, Hayakawa N, Kamiya J, Nagino M, Uesaka K. Extensive surgery for carcinoma of the gallbladder. *Br J Surg.* 2002;89:179-84.
3. Liang JL, Chan MC, Huang HY, Nq SH, Sheen-Chen SM, Liu PP, et al. Gallbladder carcinoma manifesting as acute cholecystitis: clinical and computed tomographic features. *Surgery* 2009;146:861-8.
4. Sai JK, Suyama M, Kubokawa Y, Nobukawa B. Gallbladder carcinoma associated with pancreatobiliary reflux. *World J Gastroenterol.* 2006;12:6527-30.
5. Kimura W, Nagai H, Kuroda A. Clinicopathological study of asymptomatic gallbladder carcinoma found at autopsy. *Cancer* 1989;64:98-103.
6. Indian Council of Medical Research(ICMR). Annual report of population based cancer registries of the National Cancer Registry Programme (1993). New Delhi: ICMR Publication,1996.
7. Tomohide H, Takashi W, Kenji T, Takanobu S, Haruko T, Koichiro H, et al. Spontaneous necrosis of solid gallbladder adenocarcinoma accompanied with pancreatobiliary maljunction. *World J Gastroenterol* 2008;14:5933-37.
8. Singh V, Trikha B, Nain C, Singh K, Bose S. Epidemiology of gallstone disease in Chandigarh: a community based study. *J Gastroenterol Hepatol* 2001;16:560-3.
9. Yagyu K, Lin Y, Obata Y, Kikuchi S, Ishibashi T, Kurosawa M, et al. JACC study group. Bowel movement frequency, medical history and the risk factor for gall bladder cancer death: a cohort study in Japan. *Cancer Sci* 2004;95:674-8.
10. Tanno S, Obara T, Fujii T, Mizukami Y, Shudo R, Nishino N, et al. Proliferative potential and K-ras mutation in epithelial hyperplasia of the gall bladder in patients with anomalous pancreatobiliary ductal union. *Cancer* 1998;83:267-75.
11. Hanada K, Tsuchida A, Iwao T, Eguchi N, Sasaki T, Morinaka K, et al. Gene mutations of K-ras in gallbladder mucosae and gallbladder carcinoma with an anomalous junction of the pancreatobiliary duct. *Am J Gastroenterol* 1999;94:1638-42.
12. Roa I, De Artexabala X, Araya JC, Roa J. Preneoplastic lesions in gall bladder cancer. *J Surg Oncol* 2006;93:615-23.
13. Wistuba II, Gazdar AF, Roa I, Albores-Saavedra J. p53 protein overexpression in gallbladder carcinoma and its precursor lesions: an immunohistochemical study. *Hum Pathol* 1996;27:360-5.
14. Misra S, Chaturvedi A, Goel MM, Mehrotra R, Sharma ID, Srivastava AN, et al. Overexpression of p53 protein in gall bladder carcinoma in North India. *Eur J Surg Oncol* 2000;26:164-7.
15. Jones R S. Carcinoma of the gallbladder. *Surg Clin North Am.* 1990;70:1419-28.
16. Haribhakti S P, Awasthi S, Pradeep R, Kapoor V K, Kaushik S P. Carcinoma gallbladder: atypical presentations and unusual associations. *Trop Gastroenterol.* 1997;18:32-34.
17. Rashid A, Ueki T, Gao Y T. K-ras mutation, p53 overexpression, and microsatellite instability in biliary tract cancers: a population-based study in China. *Clin Cancer Res* 2002;8:3156-63.