ULTRASONOGRAPHIC FINDINGS OF GALLBLADDER CARCINOMA

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ABSTRACT

Sonographic findings of 20 patients with histologically proven primary gallbladder carcinoma during Jan. 1996- Feb. 1999 in Lampang Hospital were reviewed. The patients were 10 women and 10 men, with age ranging from 39 to 77 years(means 64 years). Clinical manifestations included RUQ pain, jaundice, dyspepsia, weight loss and fever.

Focal or diffuse thickening of the GB wall was the most frequent sonographic findings (50%), followed by mass replacing gallbladder fossa (25%) and polypoid intraluminal mass (15%). Mass at pancreatic head region and impacted gallstone were found at equal frequency, 5% each. Associated findings were gallstones (45%), CBD stones (10%), intrahepatic duct dilatation (40%), lymphadenopathy (20%) and ascites (10%).

The histologic diagnoses were adenocarcinoma (85%), adenosquamous carcinoma (10%) and papillary adenocarcinoma (5%).

The ultimate goal of this report is to increase the general awareness of radiologists to sonographic features of GB carcinoma.

The differential diagnosis and modes of tumor spreading will be discussed.

Abbreviation: RUQ = right upper quadrant, GB = gallbladder
GS = gallstone, CBD = common bile duct, US = Ultrasonography

INTRODUCTION

Gallbladder carcinoma has a low overall prevalence.[1] It is the fifth most common malignant tumor in the alimentary tract after colorectal, pancreatic, gastric and esophageal carcinoma.[2] Predisposing factors include porcelain GB, size of the gallstone, duration of harbored stones,[3] ethnic difference ; more common in Israel, Bolivia, Chile and in south western native Americans in the united States,[4] and anomalous junction of the pancreaticobiliary duct without congenital choledochal cyst.[5] It is preferently found in female with female-to male ratios in the range of 3-4: 1, older life, mostly in the 6th decade of life or later.[1,2,6-9] Prevalence of cholelithiasis is quite high in gallbladder carcinoma, ranging from 65-98%.[10-12] It has been noted that 1 to 3 percent

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of all patients with documented gallstones will eventually have development of gallbladder carcinoma.[13] The diagnosis of gallbladder carcinoma can be made using one of the following imaging modality, US, CT, MRI, that can provide accurate staging information.[4] The objective of this study is to evaluate sonographic features of gallbladder carcinoma.

MATERIAL AND METHOD

The patients of primary gallbladder carcinoma diagnosed at Lampang hospital, during January 1996 to February 1999 were retrospectively reviewed. Patient demographic data, clinical presentations, preoperative diagnosis, detailed sonographic features and histologic findings were analyzed.

RESULTS

There were 10 females and 10 males. The ages were between 39-77 years (mean age was 64 years). Female to male ratio was 1:1. Right upper quadrant pain was the most frequent chief complaint, followed by jaundice, dyspepsia/ weight loss, positive ultrasonographic Murphy"s sign and fever (Table 1). Regarding preoperative diagnosis, gallbladder carcinoma was correctly diagnosed in half of the patients. The remaining diagnoses included gallstone with obstructed CBD stones, acute cholecystitis with gallstone, acute acalculous cholecystitis, multiple gallstones, chronic cholecystitis with gallstone, empyema gallbladder with gallstone, emphysematous gallbladder with GS, Cholangiocarcinoma with invasion of GB, mass at pancreatic head and porta hepatis (table 2).

Ultrasonography was performed in all the patients, using 3.5 MHz. Transducer; SSD 1200 Aloka. Gallbladder carcinoma appeared as focal or diffuse thickening of gallbladder wall (Fig 1-3) in 10 patients. Mass replacing GB fossa (Fig 4,5) in 5 patients. Polypoid intraluminal mass (Fig 6,7) in 3 patients. Mass at pancreatic head region and porta hepatis (Fig 8) in 1 patient. Impacted gallstones (Fig 9) in 1 patient. The first two common associated findings were gallstones and Intrahepatic bile duct dilatation. Other associated findings were lymphadenopathy, CBD stoned and ascites. Sonographic findings in GB carcinoma and associated findings are summarized respectively in Table 3. and Table 4 .

Histologic diagnoses included adenocarcinoma in 17 patients (10 well differentiated, 5 poorly differentiated, 2 moderatedly differentiated), adenosquamous carcinoma in 2 patients, and papillary adenocarcinoma in 1 patient. Histologic diagnoses are summarized in table 5.

TABLE 1. Clinical manifestations of 20 studied patients

Clinical manifestations	No (%)
RUQ pain	11 (55%)
Jaundice	8 (40%)
Dyspepsia	5 (25%)
Weight loss	5 (25%)
Positive US Murphy 's sign	4 (20%)
Fever	3 (15%)

TABLE 2. Preoperative diagnosis of studied patients

Preoperative diagnosis	No (%)
Gallbladder carcinoma	10 (50%)
Gallstones with obstructed CBD stones	2 (10%)
Acute cholecystitis with GS	1 (5%)
Acute acalculous cholecystitis	1 (5%)
Multiple gallstones	1 (5%)
Chronic cholecystitis with GS	1 (5%)
Empyema GB with GS	1 (5%)
Emphysematous GB with GS	1 (5%)
Cholangiocarcinoma with invaded GB	1 (5%)
CA head of pancreas	1 (5%)
Total	20 (100%)

TABLE 3. Sonographic findings in studied patients with gallbladder carcinoma

Sonographic findings	No (%)
Focal or diffuse thickening of GB wall	10 (50%)
Mass replacing GB fossa	5 (25%)
Polypoid mass	3 (15%)
Mass at pancreatic head region/porta hepatis	1 (5%)
Impacted gallstones	1 (5%)
Total	20 (100%)

TABLE 4. Associated findings of 20 studied patients

Associated findings	No (%)
Gallstones	9 (45%)
Intrahepatic duct dilatation	8 (40%)
Lymphadenopathy	4 (20%)
CBD stones	2 (10%)
Ascites	2 (10%)

TABLE 5. Histologic diagnosis of studied patients

Histologic diagnosis	No (%)
Adenocarcinoma	17 (85%)
Well differentiated	10
Poorly differentiated	5
Moderate differentiated	2
Adenosquamous carcinoma	2 (10%)
Papillary adenocarcinoma	1 (5%)
Total	20 (100%)

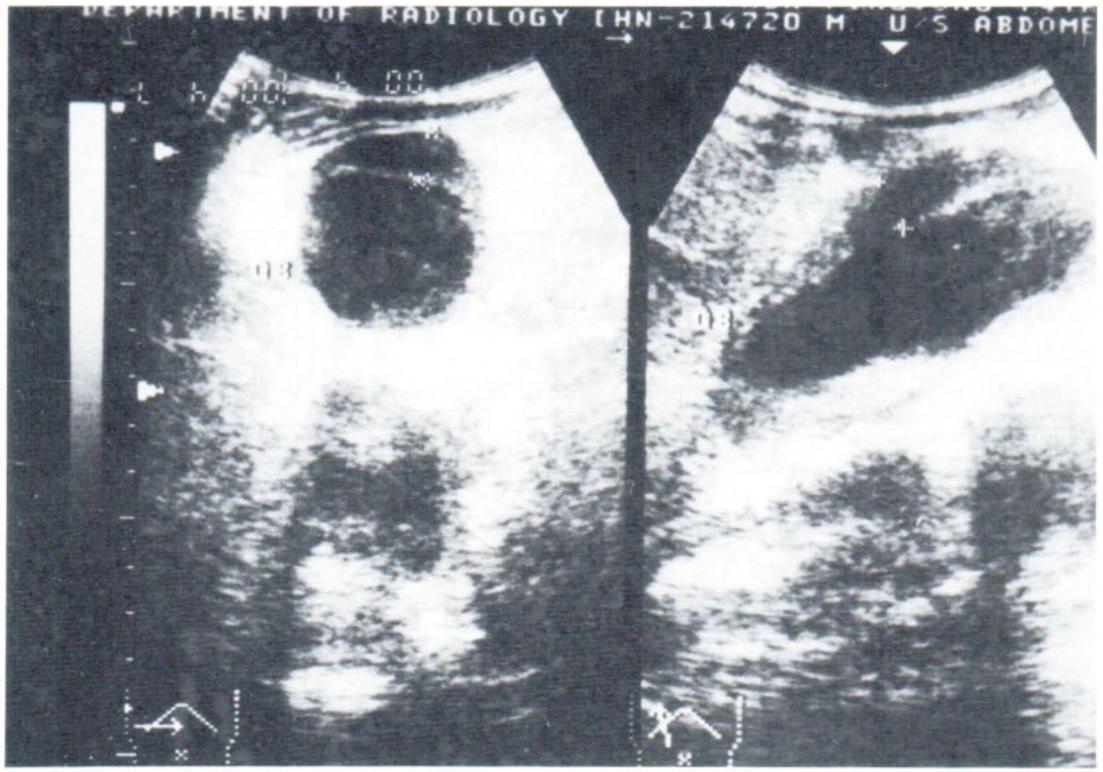

Fig. 1. Well differentiated adenocarcinoma in a 74-year-old man with RUQ pain for 3 days with fever. Transverse and longitudinal US images show non-uniform thickening of gallbladder wall without gallstone.

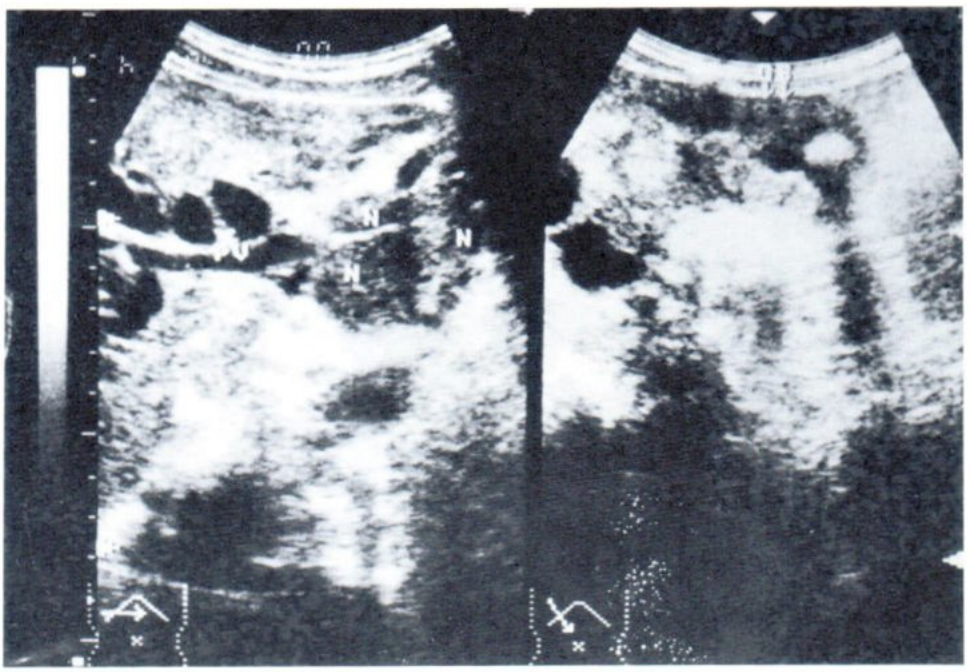

Fig. 2. Well differentiated adenocarcinoma in a 72-year-old man with dyspepsia and marked jaundice for 2 weeks. Transverse and longitudinal US images reveal enlarged porta hepatis/peripancreatic lymph nodes and diffuse GB wall thickening with gallstone.

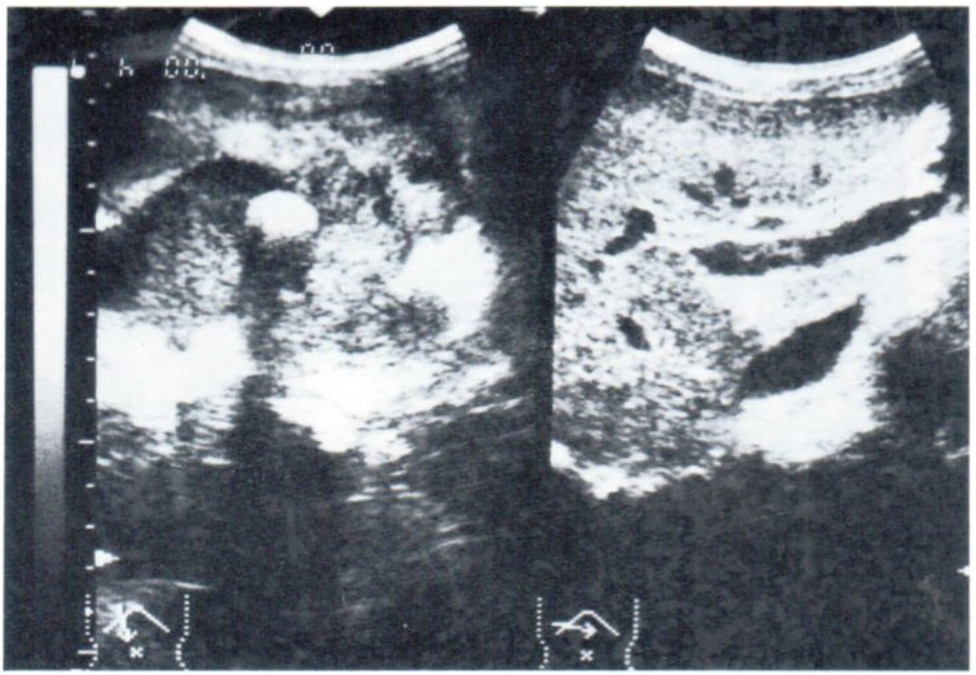

Fig. 3. A 64 -year-old man with RUQ pain and weight loss. (a) Longitudinal and transverse US images show thick irregularity of gallbladder wall with biliary sludge and gallstone without CBD dilatation.

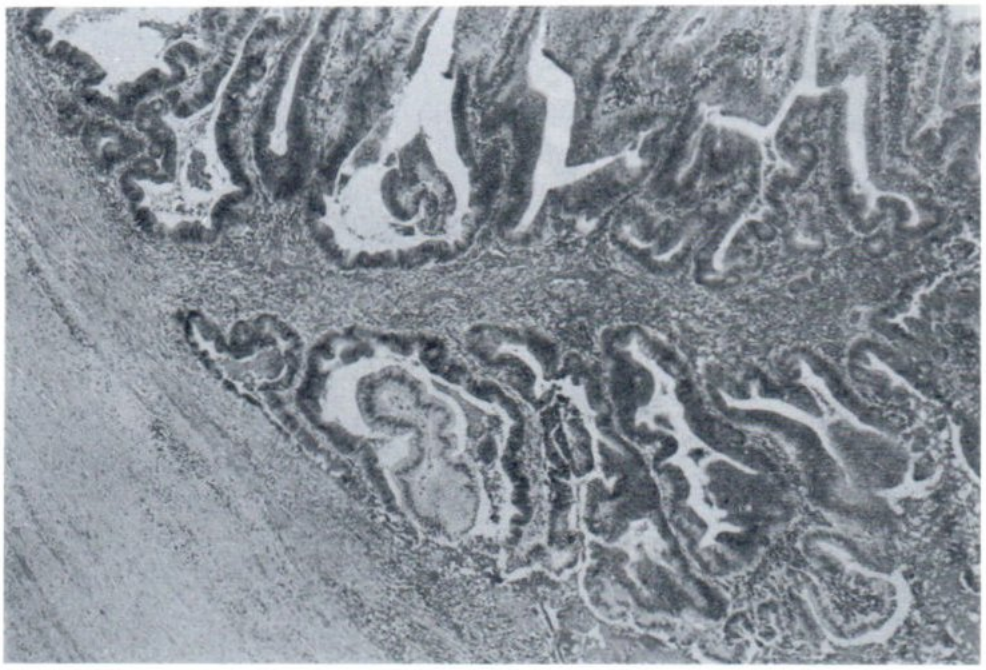

Fig. 3 b) Histology, original magnificationX100: hematoxylin-eosin stain of the tumor shows papillary adenocarcinoma ; the tumor limited to gallbladder wall.

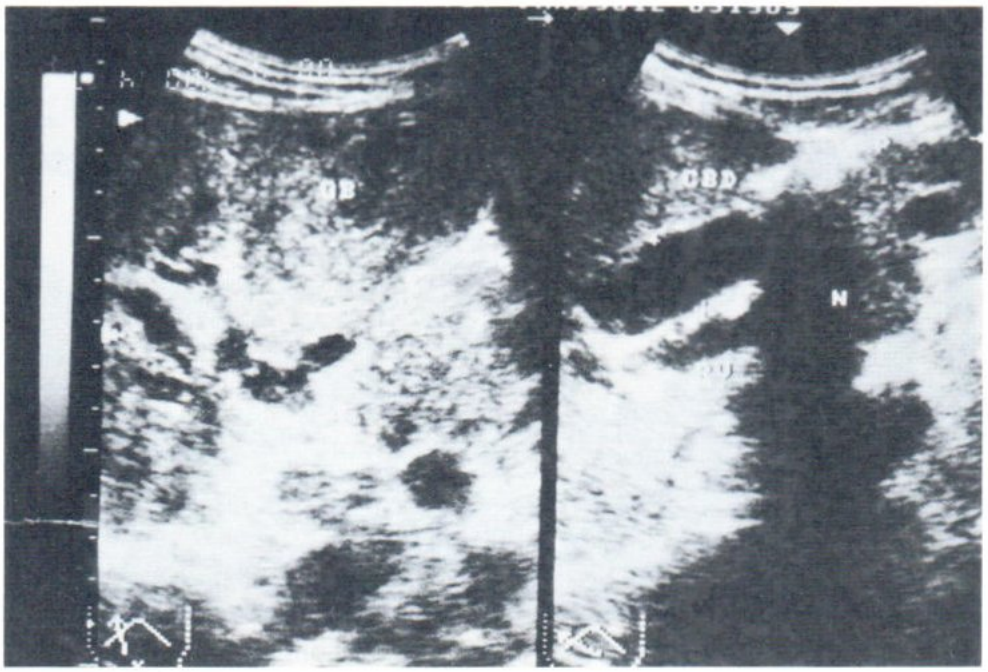

Fig. 4. A 48-year-old man with dyspepsia for 1 month and marked jaundice, 6 Kgs weight loss. (a) Longitudinal US image shows inhomogenous echogenic mass replacing GB fossa and CBD dilatation due to peripancreatic nodes.

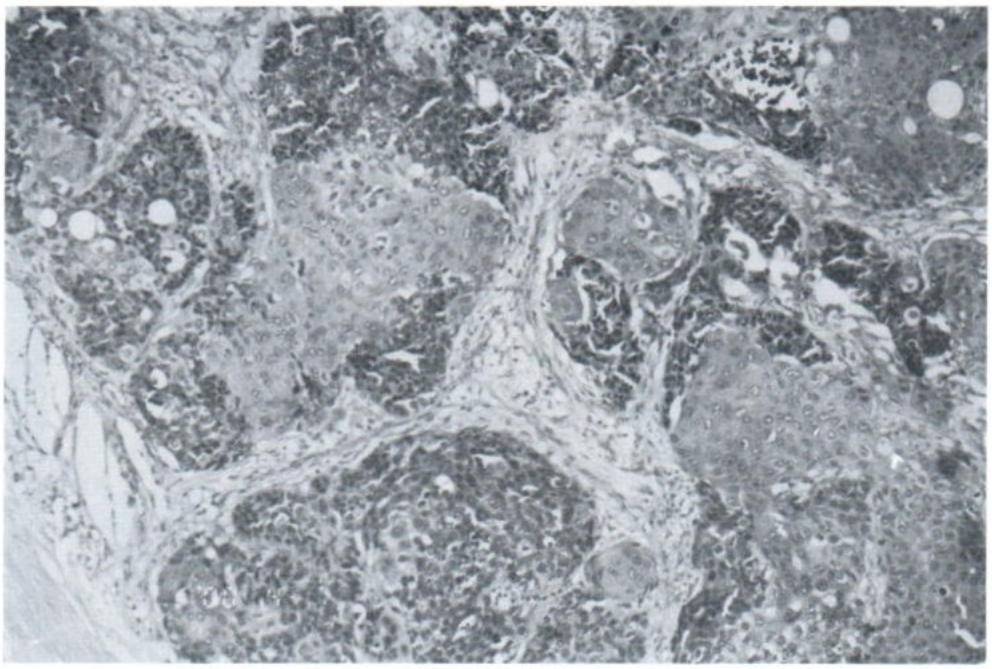

Fig. 4 (b) Histology, original magnificationX100: hematoxylin-eosin stain of the tumor shows invasive adenosquamous carcinoma.

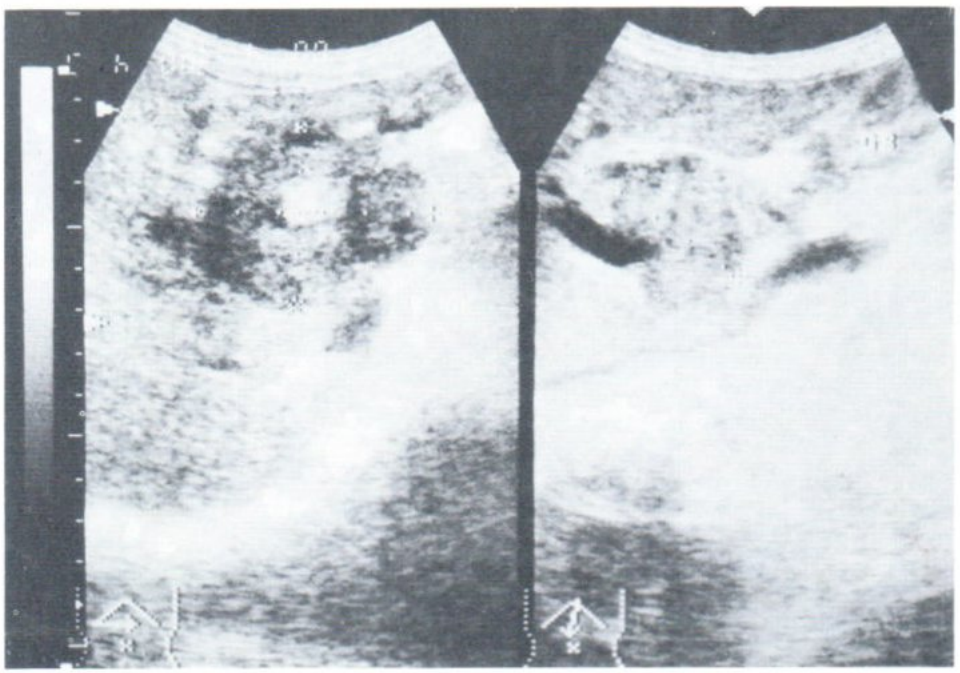

Fig. 5. Well differentiated adenocarcinoma in a 74-year-old woman with RUQ pain and weight loss. Transverse and longitudinal US images show inhomogenous mass filling the entire GB lumen with associated mass around the porta hepatis.

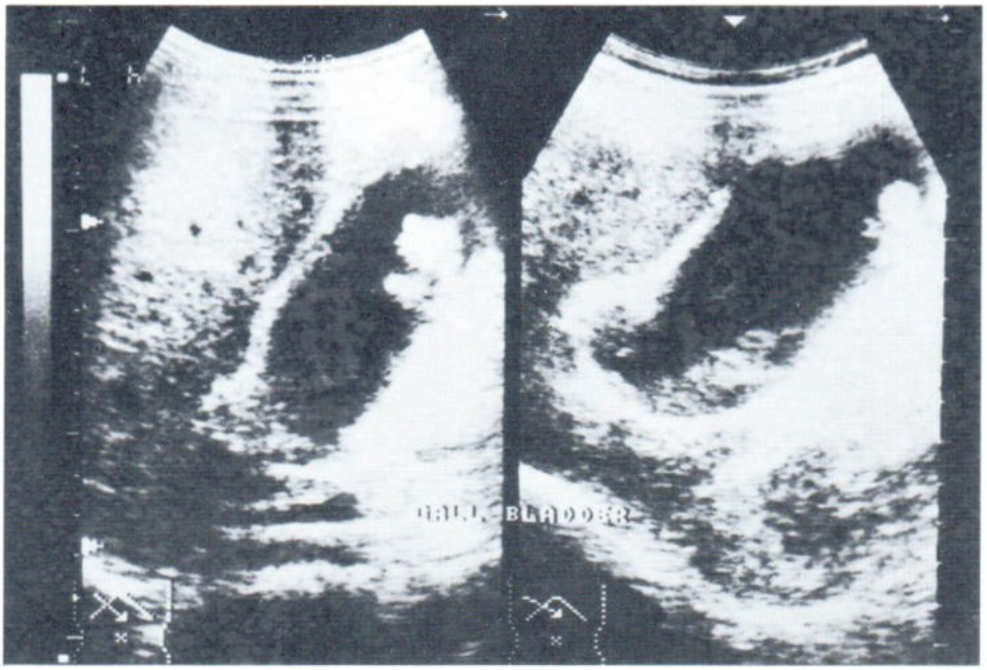

Fig. 6. A 39-year-old man with dyspepsia (a) longitudinal US image demonstrates non-movable polypoid echogenic mass extending from wall of GB near fundus.

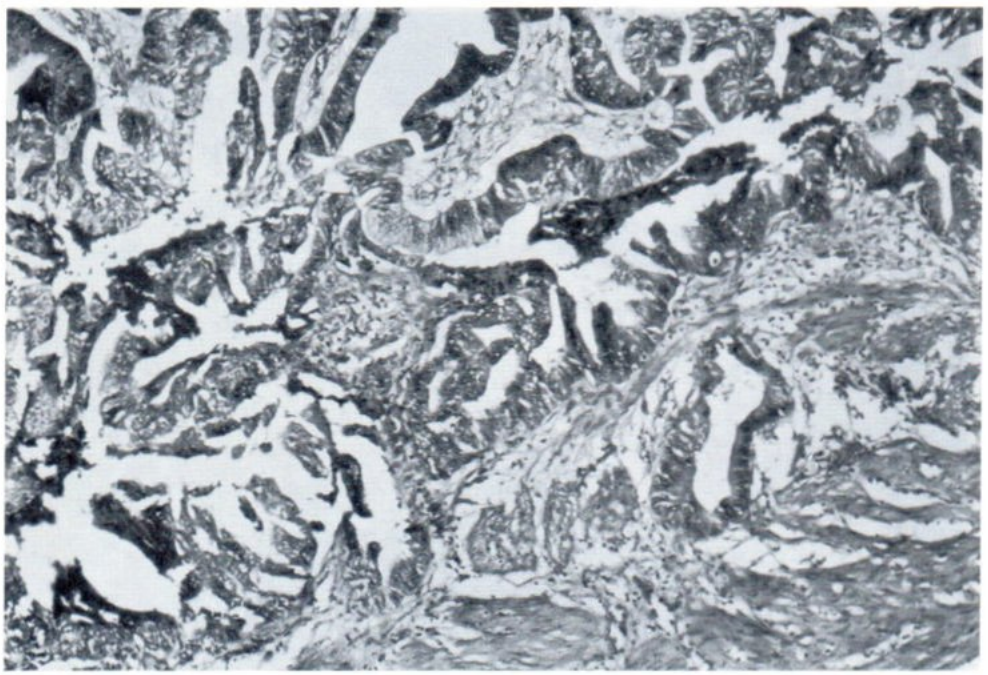

Fig. 6 (b) Histology, original magnificationX100: hematoxylin-eosin stain of the tumor shows well differentiated adenocarcinoma with transmural invasion.

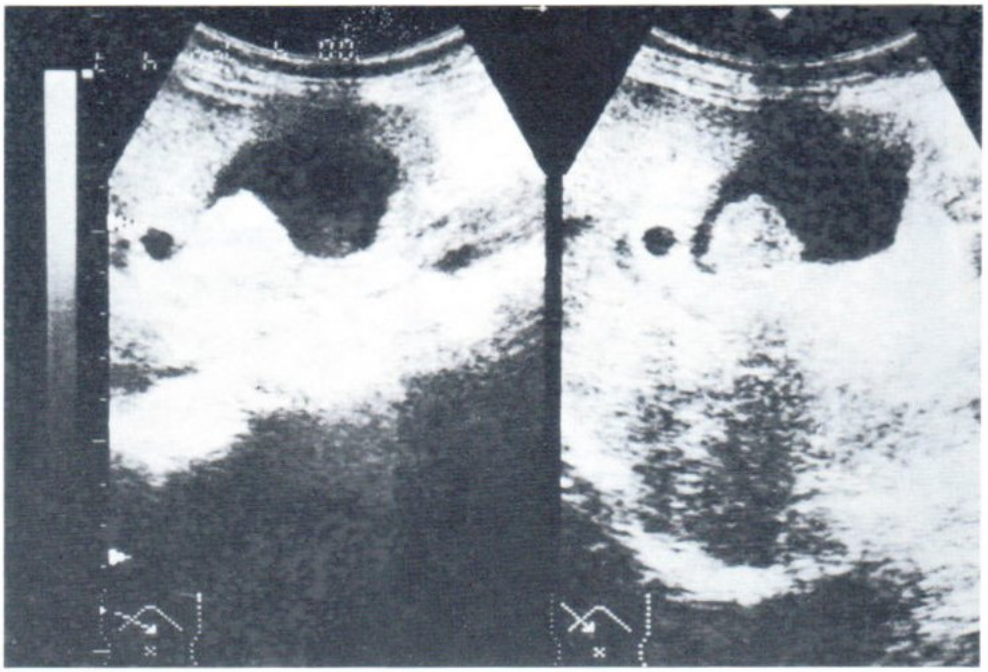

Fig. 7. Well differentiated adenocarcinoma in a 70-year-old woman with intermittent upper abdominal pain. Longitudinal US image reveals thickening of GB wall with a non-movable mass extending from GB neck.

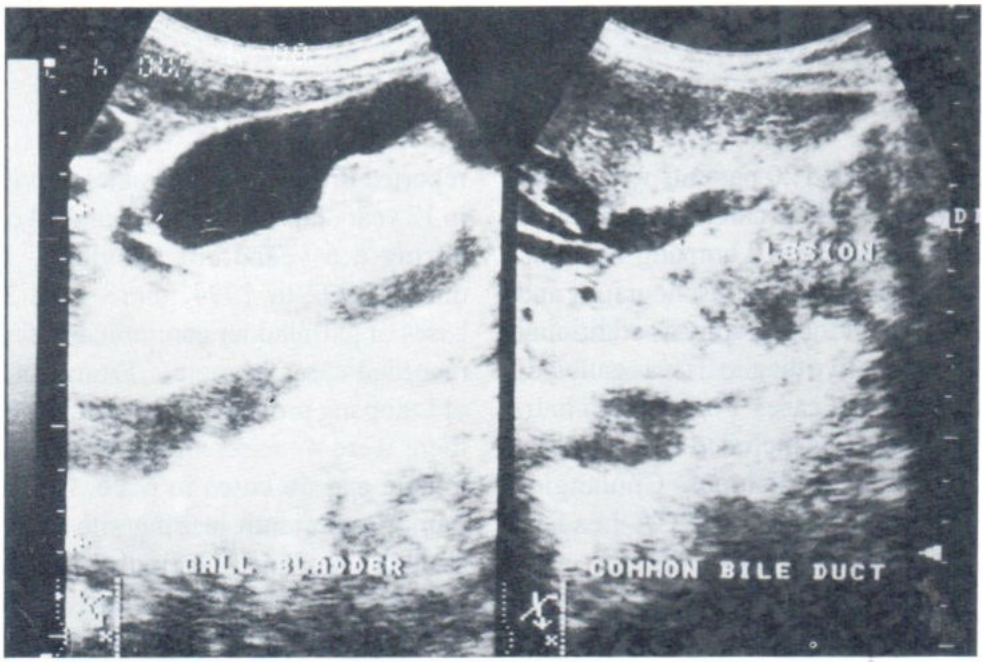

Fig. 8. Poorly differentiated adenocarcinoma in a 61-year-old woman with jaundice. Longitudinal US image shows dilated gallbladder with bile sludge and a large lobulated mass at pancreatic head region with CBD obstruction.

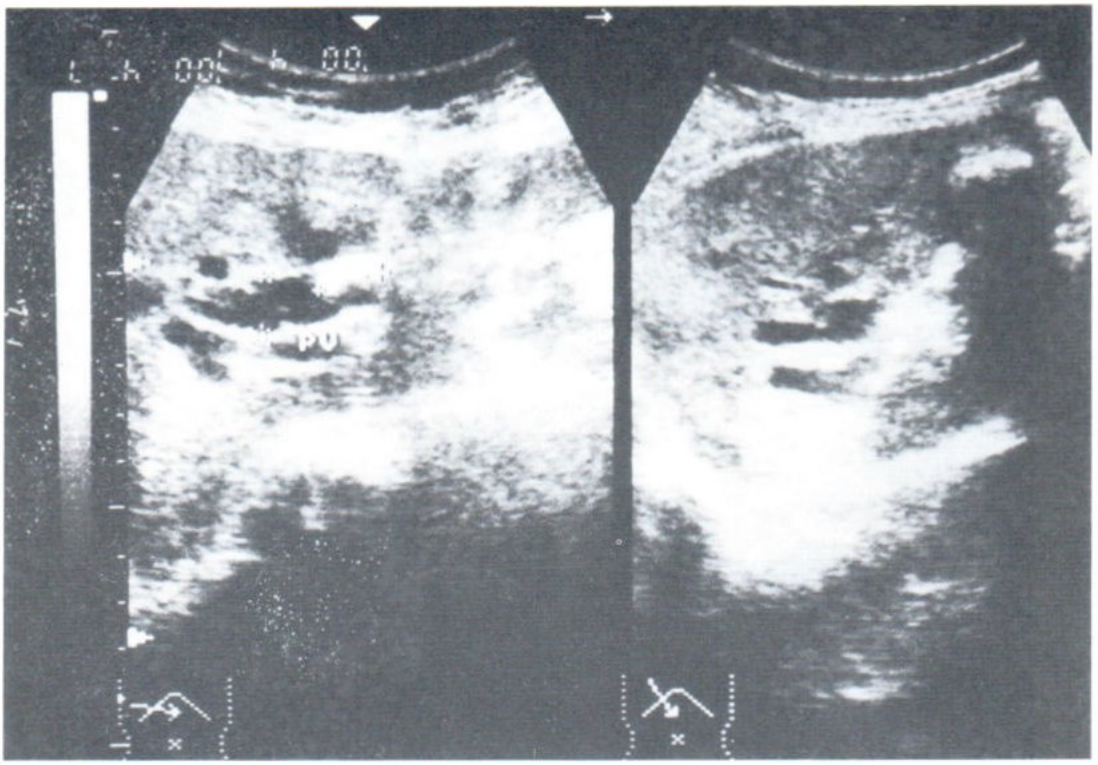

Fig. 9. Well differentiated adenocarcinoma in a 67-year-old woman with dyspepsia, jaundice and weight loss. (a)) Transverse and longitudinal US images show distal CBD stone causing CBD and intrahepatic duct dilatation as well as impacted gallstone; the detail of GB wall is not seen.

DISCUSSION

We have identified 20 patients with histologically proven gallbladder carcinoma during a period of three-year study at Lampang hospital. All 20 patients had abdominal ultrasonography and only two had computed tomography as additional investigation. Preoperative diagnosis was gallbladder carcinoma in 50% of cases. For the other half, the presumptive diagnosis included cholecystitis, obstructed CBD stone, gallstones, Cholangiocarcinoma with invaded GB and CA head of pancreas.

Gallbladder carcinoma is a rather rare malignant tumor of alimentary tract.This is supported by several previous studies i.e. 59 cases reported in a 17 year- U.S study,[14] 58 cases reported in a 14 year- Taiwanese review,[15] 44 cases in 12 year- Japanese study,[16] and 14 cases reported during a 6 year-Italian review.[17] In Thailand, during 1992 to 1994, there were 392 recorded cases of gallbladder carcinoma in female and 333 recorded cases in male.[18] From cancer incidence of Lampang province studies during 1988 to 1992, there were 42 cases of gallbladder carcinoma in female and 56 cases in male. Gallbladder carcinoma is the tenth leading site of new cancer in male in Lampang.[19] A finding of 20 new cases in a three year period of the present study support the significant incidence of this cancer in Lampang Province . This data raises at least three interesting questions. Firstly, why Thai male (in the north) has a high incidence of gallbladder carcinoma.

Secondly and thirdly, are there any predisposing factors of GB carcinoma in Lampang region and its surroundings, and what are they? Lampang Hospital is a regional center hospital located in the North of Thailand. It should be noted that Lampang province is one of a few province that have coal mines. Cooking behavior of people in the north is rather different from the other parts of Thailand. Whether or not this unique circumstance of Lampang is contributed to the high incidence of GB carcinoma remains to be studied. The equal sex distribution, in the present study is significantly different from report in the literatures. This is worthwhile to be further investigated.

Ultrasonographic and histologic findings of GB carcinoma in the present study were similar to those previously reported. However, there were some findings in this study that highly suggestive of gallbladder carcinoma. These were mass replacing GB fossa, fungate intraluminal mass with irregular border,[20] Irregularly thickened gallbladder wall, presence of lymphadenopathy and liver invasion. Findings of advanced stage were biliary dilatation, retroperitoneal lymphadenopathy, mass in porta hepatis and liver invasion. Thickening of gallbladder wall are found in many conditions such as acute, chronic,[21] emphysematous, empyematous,[22] xanthogranulomatous,[23] gangrenous cholecystitis,[24] adenomyomatosis of the gallbladder,[25] Cholesterosis, AIDS cholangiopathy.[26,27] Also other extrinsic causes such as congestive heart failure, renal failure, hypoalbuminemia,[28,29] ascites, viral hepatitis,[30] leukemic infiltration and metastasis to gallbladder.[31,32] Polypoid intraluminal mass should be differential diagnosed from cholesteral polyp as well as inflammatory polyp.[33] Other carcinomas that may mimic GB carcinoma are CA head of pancreas and cholangiocarcinoma.[34,35] Cholangiocarcinoma is more prevalence in North and Northeast of Thailand.

The most common route of tumor spreading is direct invasion into the liver. This can be explained that the hepatic surface of the gallbladder is drained by vessels communicated with adjacent hepatic veins.[36] Spread to lymph nodes around the common bile duct and other adjacent organs is also a common occurrence.[2] It should be noted that lymph node enlargement around the distal common bile duct and in the region of the head of the pancreas may be confused at sonography and CT in cases of pancreatic carcinoma.[37] Other structures that may be involved are lymph nodes in the region of the porta hepatis, hepatic and common bile ducts, pancreas, colon and duodenum.[9] Obstruction of the biliary tree results jaundice. 35-74% of patients with gallbladder carcinoma presented with jaundice at the time of admission.[37] Although jaundice is one of the earliest clinical presentations of the disease, it unfortunately signifies an advanced stage of the malignancy. In this study, 40% of patients presented with jaundice. Spread through the cystic duct and intraperitoneal seeding are encountered less often.[37] Endoscopic US is another new imaging modality, that can provide more accurate staging information, prognosis relates to depth of invasion.[38]

Prophylactic cholecystectomy is recommended for patients with anomalous pancreaticobiliary junction (APBJ) without congenital choledochal cyst, which carries a high risk of gallbladder carcinoma development. For early diagnosis of APBJ , gallbladder abnormality on ultrasonography or acute pancreatitis of unknown etiology should prompt further investigation with Endoscopic Resonance Cholangiopancreatography or less invasive imaging modalities such as endoscopic ultrasonography or MRCP (magnetic resonance cholangiopancreatography).[5]

Anomalous arrangement of the pancreaticobiliary duct is an anatomical maljunction of the bile duct and the pancreatic duct that is frequently associated with gallbladder carcinoma.

It has been postulated that pancreatic juice regurgitates into the biliary tree, and the mixture of refluxed pancreatic juice and stagnant bile juice acts as an irritant factor to the biliary tract epithelium, leading to chronic inflammation and metaplasia. Eventually these mucosal changes may progress to invasive carcinoma.[39]

CONCLUSION

Ultrasonography is a useful modality for the diagnosis of GB carcinoma ; providing critical diagnostic information which cannot be obtained by other conventional procedures. To make an early diagnosis of GB carcinoma is difficult but is essential to improve the survival of the patients with this cancer. Carcinoma tended to be missed when gallstone were present. Even in the presence of Gall stone or cholecystitis, any abnormal finding should make one suspicious of gallbladder cancer. A combination of diagnostic methods is important.

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