Role of Multidetector Computed Tomography (MDCT) in Evaluation of Gallbladder Malignancy and its Pathological Correlation in an Indian Rural Center

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ABSTRACT

Objectives: Clinically or sonographically suspected gallbladder carcinoma was evaluated on multidetector computed tomography. Based on the spectrum of multidetector computed tomography findings, staging of gallbladder carcinoma was done. Multidetector computed tomography diagnosis was compared with pathological diagnosis.

Material and Methods: This is a prospective study carried out in 100 patients at a rural Indian center between May 2012 and June 2015. Multidetector computed tomography was performed in all the cases and the findings were observed. Based on the radiological spectrum, staging of gallbladder carcinoma was done. The diagnosis was confirmed by ultrasound guided fine needle aspiration cytology/histopathological examination of surgical specimens.

Results: The most common multidetector computed tomography findings noted by us were mass replacing gallbladder, followed by diffusely focal gallbladder wall thickening and polypoidal mass. Other findings noted were cholelithiasis, liver infiltration, intra hepatic biliary dilatation, liver metastases, portal vein invasion, antroduodenal and hepatic flexure involvement. Ultrasonography guided fine needle aspiration cytology done in all cases was positive in 92 cases and inconclusive in eight cases. Surgery was performed in only 22 patients, and histopathological findings were correlated with multidetector computed tomography findings.

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Conclusion: Multidetector computed tomography is also reliable in detection of extension of tumor and lymph nodes. multidetector computed tomography plays a major role in evaluating and staging of carcinoma gallbladder. It also guides the surgeons for operability and resectability of tumour.

Keywords: gallbladder, carcinoma, multidetector computed tomography, fine needle aspiration cytology, surgery.

INTRODUCTION

Carcinoma of the gallbladder (GB) is the most common biliary tract malignancy and is the fifth most common malignancy of the alimentary tract. Gallbladder cancer, although rare in Caucasian population, is among the most frequently observed cancers in the population of Indian subcontinent. The highest incidence of GB carcinoma in India was seen along the Ganges delta (1). In all populations, there is a strong correlation between gallstones and GB cancer: the risk of GB cancer is approximately 4-5 times higher in patients with gallstones than in those without gallstones (73-98%). History of biliary disease, elderly female, obesity, high carbohydrate diet, ethanol abuse and tobacco abuse, all of which are associated with calculus biliary disease, have been shown to be associated with a higher risk for the development of GB cancer. Mirizzi's syndrome has also been associated with an increased risk of GB cancer. Other risk factors include porcelain GB, choledochal cysts, anomalous pancreaticobiliary duct junctions, and GB polyps >1 cm in size (2). Gallbladder carcinoma has a peak incidence in the sixth and seventh decades of life and is three to five times more predominant in females.

Early-stage carcinoma is typically diagnosed incidentally because of inflammatory symptoms related to coexistent cholelithiasis or cholecystitis. Jaundice occurs more frequently as a result of malignant obstruction of the biliary tree rather than hepatic metastasis or coexistent choledocholithiasis (3). Multidetector computed tomography (MDCT) plays an important role in the diagnosis and staging of GB carcinoma for the purpose of management (4). We present MDCT spectrum of a large series of patients with GB carcinoma studied prospectively. □

MATERIALS AND METHODS

This was a prospective study that was carried out on one hundred selected patients with GB carcinoma over a period of three years between May 2012 and June 2015. The study was completed in a rural Indian center. Ethical clearance was taken from the institutional committee as IEC/MMIMSR/15/146. Subjects included in this study were referred from Medical OPD, Surgical OPD or admitted in the respective wards with clinical suspicion of GB malignancy or GB malignancy found incidentally on ultrasonography (USG). Informed consent was taken from all patients.

A complete history, detailed clinical examination was performed in all cases. Routine laboratory investigations like haemoglobin, total leucocyte count, differential leucocyte count were carried out in all patients. Biochemical investigations relevant to the diagnosis of GB carcinoma, such as liver function tests, were done, USG examination was performed in all patients and findings were duly recorded.

Contrast enhanced computed tomography (CECT) scan was done in all patients on Ingenuity CT (64 MDCT, Philips Medical Systems), using oral and I/V contrast agents. Oral contrast (30 mL of Diatrizoate Megluminate 66% diluted with 1000 mL of water) was used for bowel opacification, and 80 mL of non-ionic contrast (Iohexol) containing 300 mg/mL of iodine were administered as a single bolus.

Non-contrast CT and biphasic/triphasic contrast enhanced CT was done. Multiplanar coronal and sagittal sections were taken. Thin Axial CT sections and multiplanar reconstructed sections were studied in detail. Findings such as mass replacing GB, intraluminal polypoid lesions, focal or diffuse asymmetric wall thickening of the gallbladder, associated GB calculi and lesions in the hepatic area, any lymphadenopathy or associa-

ted lesions were noted. Based on detailed CT findings, the staging of the GB carcinoma was established. Ultrasound guided fine needle aspiration cytology (FNAC) was done in all cases. Surgery was performed in 22 cases and histopathological examination (HPE) of specimens was obtained. □

RESULTS

Various parameters as described in the section of materials and methods were studied and observations were recorded. Age distribution in our series ranged from 33 to 82 years. Maximum number of patients (31%) was in the age group of 61-70 years. Second highest incidence was in the >70 year age group (29%), followed by 51-60 year age group (23%). Out of the 100 patients included in the study, 60 (60%) were females and 40 (40%) males, with a female to male ratio of 1.5:1.

The predominant clinical symptom was abdominal pain, followed by abdominal lump, jaundice, anorexia and weight loss. Abdominal pain was seen in 71 (71%) patients, who were in the form of dull aching or colicky pain in the right upper quadrant in majority of cases, abdominal lump was present in 34 (34%) patients and jaundice in 40 (40%). Thus, on initial presentation, the pain associated with GB carcinoma could not be distinguished from that of gallstone disease.

Various investigations were done. Serum proteins were low in 60% of patients. Those with abnormally raised liver enzymes also had hyperbilirubinemia, which was present in 57% of all patients. Thus, in majority of cases, obstructive jaundice was present. Forty three (43%) patients were anemic.

Out of 100 cases in our study, the commonest MDCT finding was mass replacing GB (63%), i.e. the whole of the gallbladder was replaced by mass and the GB was not separately visualised, followed by diffuse/focal GB wall thickening (26%) (Figures 1 and 6), i.e. thickening of GB wall, which was irregular and showed an enhancement on CECT and polypoidal mass in (11%) cases (Figures 2 and 6).

Associated CT findings noted by us were represented by liver infiltration, which was seen in 81 patients. In 65 of them, liver infiltration was limited to segments IV A and V of the liver, and in 16 patients, infiltration extended to other seg-

FIGURE 1. a) Axial CECT showing diffuse irregular thickening of gallbladder wall (black arrow) with heterogenous enhancement and ascites; b) axial CECT in the same patient showing ascites with nodular peritoneal thickening in perihepatic region (black arrow) and IHBR dilation

FIGURE 2. a) Image showing mass in fundus region (black arrow) with liver infiltration (white arrow); b) lower axial section in the same patient, showing cholelithiasis (thick black arrow), para-aortic lymphadenopathy (white arrow) and renal deposit (thin black arrow)

FIGURE 3. a) Coronal section showing heterogeneous mass in the body and neck of the gallbladder (white arrow), causing a mass effect on CBD with resultant upstream IHBR dilatation (black arrow); b) coronal section showing mass in gallbladder (black arrow) with duodenal infiltration (white arrow)

ments too. Intra hepatic biliary dilation was noted in 63 cases (Figures 1 and 3). Cholelithiasis was associated in 55 (55%) patients (Figures 2 and 4).

Liver metastases were present in 33 cases and portal vein invasion in 11 cases (Figure 5). Lymph node metastasis was noted in 74 cases (Figure 2). Antroduodenal and hepatic flexure involvement was seen in 18 cases (Figure 3). Peritoneal involvement with ascites was seen in 30 cases with Krukenberg's deposits (Figure 5) in bilateral ovaries of six patients, and pleural effusion in 11 cases (Figure 6).

FIGURE 4. a) CECT showing mass lesion (black arrow) in fundus of gallbladder; b) surgical specimen of the same patient showing mass in fundus, gall stones, resected liver margin

FIGURE 5. a) Coronal section in showing liver metastases (black arrow) and ascites (white arrow); b) coronal section showing bilateral bulky adnexae with heterogenous enhancing solid and cystic components – Krukenbergs deposits (black arrow) with ascites

Ultrasonography guided FNAC was done in all cases. It was positive in 92 cases and inconclusive in eight cases. In 82 of all 92 patients, it showed malignancy of the GB and in 10 patients benign pathology.

Surgery was performed in only 22 patients because most of our cases were either in advanced stage or did not turn up for follow up. Specimens of these 22 cases were sent for histopathology. On histopathology, 17 cases were found to be malignant and five benign. Of the 17 malignant cases, 15 were adenocarcinoma and two adenosquamous carcinoma of the GB.

Regarding 'T' staging of patients, none of the patients was in T1 stage; T2 stage was seen in 17 patients, whereas T3 and T4 stages were found in 41 and 24 patients, respectively. Maximum number of patients had advanced disease at the time of presentation.

Metastatic lymph nodes were seen in the region of cystic duct, pericholedochal, or at porta (N1) in 48 patients. Peripancreatic (head only), periduodenal, celiac, or superior mesenteric lymph nodes (N2) were found in 26 patients. The maximum number of patients had N1 stage.

FIGURE 6. a) Pie chart showing the type of lesion on CECT; b) bar diagram showing associated CT findings in patients with GB mass on CECT

Thirty five patients had distant metastasis and were in M stage, according to AJCC (American Joint Committee on Cancer) Gallbladder Carcinoma Staging. Out of all 100 cases, 82 were proven to have GB carcinoma based on cytology and histopathology. □

DISCUSSIONS

Gallbladder carcinoma is the commonest malignancy of the biliary system and the fifth most common intra-abdominal malignancy. It has a varying demographic distribution in different parts of the world as well as in our country. It is a common cancer in the Ganges belt of North Eastern India and is due to high concentrations of heavy metals in water and soil of villages along the Indo-gangetic plains (5). Its incidence in this region is one of the highest in the world.

There is an opportunity to identify the presenting symptoms and early findings on USG and CECT for early diagnosis of this dreaded disease. Unfortunately, our patients present very late due to their socio-economic status. Sonography is usually the most common imaging test to evaluate symptoms of biliary tract disease, including suspected GB carcinoma. With recent advances in imaging modalities such as MDCT scanners, magnetic resonance imaging (MRI), positron emission tomography (PET)/CT, diagnosis of GB cancer has improved. Multidetector computed tomography has the advantages of multiplanar imaging and better resolution over conventional CT. However, studies have shown that combined dynamic CT scan and ultrasound can clearly show the local anatomy of GB and bile ducts as well as the liver and adjacent organs (6). Studies have also targeted molecular and genetic pathways. Treatment options have included extended and radical surgeries with adjuvant chemotherapy.

Age group in yrs	No. of cases	Percentage
< 50	17	17
51-60	23	23
61-70	31	31
>70	29	29

TABLE 1. Age distribution of patients

The present study was conducted on 100 cases with clinically suspected GB malignancy and gallbladder masses that were found incidentally on USG. Clinical features, radiological findings and pathological investigations were studied in these patients. In the present study, age distribution ranged from 33 to 82 years. Male to female ratio in our series was 1:1.5. Pain was the predominant symptom in most of our patients, followed by jaundice and weight loss.

Gallbladder carcinoma may appear as a mass completely replacing the GB (40-65%), a focal or diffuse asymmetric GB wall thickening (20-30%), or intraluminal polypoid lesion (15-25%). In our study, a mass replacing the entire GB was seen in 62.8% of patients, asymmetrical wall thickening of the GB in 45% of patients, and polypoidal intraluminal mass in 11.4% of patients. Associated cholelithiasis was seen in 55.2% of all cases, which was comparable to the study done by Dwivedi *et al*, who reported cholelithiasis in 48.3% of patients (7). However, the study conducted by Sachidananda *et al* (8) showed that GB carcinoma was uncommon in South India and association with cholelithiasis was also low (19.6%). Amongst the associated findings, liver infiltration was the most common, as observed by us and other authors (7). The spread of GB carcinoma to the liver and adjacent organs is facilitated by the lack of a muscularis mucosa and submucosa in the GB wall and its direct venous drainage through the liver parenchyma to the hepatic veins.

Duodenal and hepatic flexure involvement was seen by us in 18.5% of cases. Dwivedi *et al* (7) and Kalra *et al* (9) reported such invasion in 41.4% and 8.3% of their cases, respectively. Portal vein thrombosis was seen in 11% of our cases, which is comparable to Dwivedi *et al* (7) series (12.6%), while Kalra *et al* (9) reported a higher association of portal vein thrombosis (20%).

Lymphatic drainage from the GB occurs in a predictive fashion and correlates with the pattern

Type of lesion	No of cases	Percentage
Mass replacing GB	63	63
Wall thickening	26	26
Polypoidal mass	11	11
Total	100	100

TABLE 2. Details of lesions

of lymph node metastasis seen in GB carcinoma. Initially, cystic duct and pericholedochal nodes are involved, followed by distant metastasis to nodes to the head of pancreas and then to aorto-caval nodes. Low sensitivities have been reported for the detection of positive nodes on CECT. However, involvement of N1 or N2 nodal stations is not a criterion for non-resectability of GB carcinoma. In the present study, N spread was comparable to Kalra *et al*'s series (9).

Tumor staging is the main part for the management of GB carcinoma. AJCC has given the TNM staging system, which usually defines, and is determined by, the depth of invasion, extension into adjacent structures, lymph node involvement and metastatic spread. The primary stage of GB carcinoma, which decides the treatment, is the "T" stage. Surgery is usually performed for T1/T2 (tumors confined to GB wall). Tumors extending beyond the GB wall are considered T3 and T4. T3 tumor can be resected with en bloc and resection of adjacent organ, whereas T4 tumors are unresectable. According to AJCC, primary GB carcinoma has been classified as T1, confined to *lamina propria* or the muscle layer of the GB (T1A and T2B, respectively), T2 extending to serosa, T3 perforating the serosa or directly invading the adjacent structure, T4 invading the main portal vein, hepatic artery or distant organs.

In the present study, we followed the CT criteria for T staging as defined by Kim (10) for the purpose of management. According to these criteria, T1 is the polypoidal lesion without GB thickening wall, and T2 is nodular or sessile lesion associated with focal thickening of the GB wall. The remaining staging was similar to AJCC's description.

The prognosis for GB carcinoma remains poor because most gallbladder carcinomas present when the disease has an advanced stage and the curative resection rate ranges only between 10% and 30%. Given that surgery is the only definitive

curative therapy and the extent of surgery is determined by the magnitude of local tumor spread, it is important to diagnose this disease in an early stage and to accurately determine its extent. For this purpose, several imaging techniques such as CT (computed tomography), MRI (magnetic resonance imaging), PET-CT (11) and endoscopic sonography are currently being used, with CT being the most commonly used imaging study. □

CONCLUSION

Multidetector computed tomography is reliable in the detection of a primary GB malignant mass and in assessing the local exten-

sion of tumor into the liver. It is also reliable in detection of tumor extension to distant sites and lymph nodes. Indians are ethnically and culturally different from their Western counterparts among whom the incidence of this disease is comparatively low. Dual-phase MDCT coupled with 3D volume-rendered reconstruction is a comprehensive preoperative imaging technique for gallbladder carcinoma. It helps to determine the resectability of GB carcinoma and provides a vascular road map for radical cholecystectomy. □

Conflicts of interest: none declared.

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