

Role of CT/MRI in Diagnosis of Gallbladder Malignancy

Naveen Sheelavant¹, Ravi Kumar Yeli¹, Naga Babu Pyadala²

¹Assistant Professor, Department of Radiology & Imaging, B M Patil Medical Collage & Research Centre, BLDE University (DU), Vijayapur, Karnataka, ²Associate Professor, Department of Biochemistry, MNR Medical College & Hospital, Sangareddy, Telangana, India

Corresponding author: Dr. Ravi Kumar Yeli, Assistant Professor, Department of Radiology & Imaging, Shri B M Patil Medical Collage & Research Centre, BLDE University (DU), Ashram Road, Vijayapur, Karnataka - 586103, India

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A B S T R A C T

Introduction: Gallbladder cancer carries an extremely high mortality rate, with a 5-year survival rate as low as 12%. Survival is dependent on the diagnosis of these tumors in their earliest stages. This study sought to describe the clinical and imaging features of stages T1, T2, and T3 gallbladder tumors and to illustrate features that may allow radiologists to make an early diagnosis.

Material and Methods: After approval from the institutional review board, a search of the pathology department database yielded 16 patients with surgically proven T1, T2, and T3 gallbladder cancers with available preoperative computed tomography (CT) or magnetic resonance imaging (MRI). The imaging was reviewed for lesional morphology (focal polypoid mass, focal wall thickening, circumferential wall thickening), enhancement characteristics, liver invasion, locoregional lymphadenopathy, and distant metastatic disease. The electronic medical record was also searched for demographic information and clinical presentation.

Results: There was 9 women and 7 men with a mean age of 67 years. Virtually all patients were symptomatic, with most patients demonstrating symptoms suggestive of underlying malignancy (including jaundice, weight loss, and chronic abdominal pain). Tumors on CT and MRI included 6 polypoid masses, 7 tumors with focal wall thickening, and 3 with circumferential wall thickening.

Conclusion: The imaging findings of gallbladder cancer can be subtle, regardless of whether the tumor presents as a discrete mass, focal wall thickening, or circumferential diffuse wall thickening, and radio-logists should be aware of the wide range of different possible appearances. Moreover, the vast majority of these patients had clinical symptoms suggestive of an underlying malignancy, and this should precipitate a careful evaluation of the gallbladder in all such cases.

Keywords: Gallbladder Carcinoma, Computed Tomography, Magnetic Resonance Imaging.

INTRODUCTION

Although a relatively rare malignancy, gallbladder cancer is the fifth most common tumor of the gastrointestinal tract and still accounts for more than 60% of all biliary tract malignancies, with more than 6000 new cases diagnosed in the United States in 2012.¹⁻³ Gallbladder carcinoma carries an extraordinarily poor prognosis, even in those patients who undergo surgical resection with a curative intent, with 5-year survival rates as low as 12%.⁴ This poor prognosis stresses the importance of identifying these carcinomas in their earliest stages because patients with T1 (tumors confined to the lamina propria or muscular layer of the gallbladder wall) and T2 (tumors extending into the muscularis mucosa) lesions have a much better prognosis compared with patients with T3 or T4 lesions (tumors no longer confined to the gallbladder).⁵⁻⁷ Tumors that are found in their earliest stages can often be treated with a simple or extended cholecystectomy, and patients have a better chance for long-term survival. On the other hand, only 10% to 30% of patients

with advanced stage gallbladder cancer are candidates for curative resection, and those patients who are still surgical candidates require much more extensive surgical resections.² Unfortunately, the prospective identification of these lesions using cross-sectional imaging techniques remains very difficult, and many of these tumors are incidentally found either on autopsy or during cholecystectomy for another indication.⁸ In many cases of gallbladder cancer, the imaging findings can be extraordinarily subtle and difficult to perceive for the radiologist, and prospective identification of these malignancies requires an understanding of the most common appearances and clinical presentations of these lesions while still in their earliest stages. As a result, this study sought to retrospectively evaluate the imaging appearance on computed tomography (CT) and magnetic resonance imaging (MRI) of patients with T1, T2, and T3 gallbladder cancers.

MATERIAL AND METHODS

Our institutional review board approved the study, and we

received a waiver of informed consent for review of both clinical records and any prior imaging examinations. A search of the pathology department database was then conducted, yielding 16 patients with pathologically proven T1, T2, or T3 gallbladder cancer and with imaging available on picture archiving and communication system (PACS) at our institution (either CT or MRI). Patients with T4 gallbladder cancers were excluded from the study. Once the patients were identified, the electronic medical record was then reviewed for clinical and demographic information, including patient age, sex, presenting symptoms, and the like. In addition to retrospective CT and MRI review, the original dictations for

each of the patients' preoperative imaging examinations were also reviewed to ascertain whether the patients' gallbladder cancers were diagnosed prospectively (including CT, MRI, and ultrasound). The available CT and MRI examinations (16 patients with only CT, 2 patients with only MRI) for each patient were interpreted by a board-certified radiologist with subspecialty training in abdominal imaging and 2 years of experience after fellowship. Each of the studies (regardless of the imaging modality) was interpreted with regard to the following features: (a) presence of gallstones, (b) presence of focal gallbladder thickening (including the length and thickness of that abnormality), (c) presence of diffuse gallbladder wall thickening (including measurement of thickness), (d) presence of a focal mass within the gallbladder (including size of that mass), (e) Hounsfield attenuation measurements in any available phases of imaging (on CT), (f) presence of suspicious locoregional lymphadenopathy, (g) assessment of possible liver invasion, (h) presence of peritoneal or omental implants/carcinomatosis, and (i) evidence of superimposed cholecystitis.

RESULTS

Patient demographics (age, sex) and presenting symptoms are listed in Table 1. The patients were relatively equally divided by sex (9 women, 7 men), and the mean age at presentation was 67 years. Of the 15 patients for whom preoperative notes were available, the most common presenting symptom was jaundice (10 patients). Whereas most of the patients had symptoms at least suggestive of malignancy, 2 patients presented only with acute abdominal pain. Pathologic staging information, the time between surgery and imaging, and follow-up information are listed in Table 2. Notably, 2 of the 4 patients who were initially found to have distant metastatic disease at presentation had their metastases (carcinomatosis) discovered only at surgery. Three of these 4 patients had T3 tumors (1 was T2). Four patients later developed distant metastatic disease, all of whom had T3 tumors. Five patients had evidence at pathology of direct tumor invasion into the liver, 3 of which were correctly identified on preoperative CT. Three additional patients were incorrectly thought to have liver invasion on the basis of CT. The MDCT imaging data are presented in Table 3. 4 patients presented with a discrete polyploid mass, 9 patients presented with focal wall thickening, and 3 patients presented with diffuse circumferential wall thickening. Seven patients were thought

Category	Total numbers
Men	7
Women	9
Mean age	67 years
Weight loss	2
Chronic abdominal pain	3
Acute abdominal pain	2
Jaundice	10
Nausea and vomiting	1
None	1
Unknown symptoms	1

Table-1: Demographic and Clinical Information of Gallbladder Cancer patients (n= 16).

Category	Total
T1	2
T2	4
T3	10
T4	0
N0	2
N1	8
M0	14
Mx	2
Time between imaging and surgery mean	0-0.071
No. patients without distant metastatic disease at the last follow-up	9
No. patients who developed metastatic disease after surgery	3

Table-2: Pathologic findings of gallbladder cancer patients (n= 16).

Category	Total
Polyploid mass	4
Focal wall thickening	9
Diffuse circumferential wall thickening	3
Size of polyploid masses	15-61 mm
Wall thickness for tumors presenting as circumferential wall thickening, mean/median (range)	9-23 mm
Wall thickness for tumors presenting as focal wall thickening, mean/median (range)	8-24 mm
Length of thickening for tumors presenting as focal wall thickening, mean/median (range)	13-80 mm
Hounsfield attenuation tumor arterial phase	25-108
Hounsfield attenuation tumor venous phase	33-219
Change in attenuation (venous-arterial)	5-129

Table-3: Imaging Findings for the 16 Patients with Preoperative CT or MRI.

to have suspicious locoregional lymphadenopathy (based on size, morphology, or central necrosis): 4 of these patients were found to have malignant lymphadenopathy at lymph node dissection, whereas the other 3 patients did not undergo lymph node sampling at surgery. Two patients were correctly identified as having distant metastatic disease on preoperative imaging (1 with carcinomatosis, 1 with liver metastases), whereas carcinomatosis found at surgery was not perceived on 2 other CT studies. Four patients were found to have gallstones on CT. Enhancement increased from the arterial to venous phases in all cases with dual-phase imaging. The mean attenuation of those tumors imaged with CT was 59.4 on the arterial phase and 86.5 on the venous phase, with a mean increase in Hounsfield attenuation between the arterial and venous phases of 28.2 HUs.

DISCUSSION

Gallbladder cancer carries a dismal prognosis, with an overall survival rate reported as low as 12%.^{4,5} Virtually, all survivors of this tumor harbor a lower stage of disease, and patients with more advanced tumors (higher stage) have extremely low survival rates.⁵ The T stage of these tumors carries great significance in terms of both prognosis and treatment: T1 lesions, which are confined to the lamina propria or the muscular layer of the gallbladder wall, can usually be treated adequately with a simple laparoscopic cholecystectomy.⁷ T2 tumors, which have grown into the perimuscular fibrous tissue/muscularis mucosa, are typically treated with extended cholecystectomy or even more extensive surgeries.⁹ T3 (tumors that have grown into the serosa and/or directly into either the liver or other adjacent structures) and T4 (tumors with vascular involvement, more than 2 cm of invasion into the liver, or involvement of 2 or more structures other than the liver) tumors carry an extremely poor prognosis, and although many of these tumors may be unresectable, radical resection is necessary in those cases with a potentially resectable tumor. Although our study population was small, it generally supported the poor prognosis of these tumors, with 4 and 9 patients (of 16) demonstrating metastatic disease and malignant locoregional lymphadenopathy at presentation, respectively, and an additional 4 patients developing progressive metastatic disease during the course of their follow-up. Notably, however, of the 7 patients with T1 and T2 tumors, only 1 demonstrated distant metastatic disease and 3 demonstrated locoregional lymphadenopathy at presentation (and none during the follow-up), underscoring the importance of identifying these tumors early in their course. It is important to recognize that, in the vast majority of these cases, the patient's clinical presentation should have alerted the radiologist to be vigilant about the presence of malignancy: The most common clinical presentations included jaundice, weight loss, and chronic abdominal pain, all histories suggestive of underlying malignancy. Despite this, 2 patients presented with acute abdominal pain and 1 patient had no appreciable symptoms, such that the absence of an appropriate history cannot necessarily exclude the presence of a cancer. The accuracy of CT in the diagnosis of gallbladder cancer has previously been reported as 84% to 92%, with sensitivities and specificities ranging from 73% to

87% and 88% to 100%, respectively.¹⁰⁻¹² Features that have been previously described as suggestive of a gallbladder malignancy on CT include a discrete focal gallbladder mass, irregular focal wall thickening, and a "2-layer pattern" of enhancement in a thickened gallbladder wall (with a weakly enhancing outer layer and a strongly enhancing, thickened inner layer).^{11,13} On the other hand, the performance of MRI in the diagnosis of gallbladder cancer has not been well established, although suggestive features are similar to those on CT, including a focal mass, focal gallbladder wall thickening, abnormal enhancement, and restricted diffusion (low apparent diffusion coefficient values).^{9,14,15} The results of this study support a wide range of different possible imaging appearances for gallbladder cancer, with 4 polyploid masses, 9 cases with focal wall thickening, and 3 cases with diffuse circumferential wall thickening. Interestingly, given the large number of other potential causes for diffuse circumferential wall thickening, including cholecystitis, adenomyomatosis, intrinsic liver disease, congestive heart failure, and renal failure, diffuse wall thickening has traditionally not thought to be suggestive of malignancy.^{16,17} Of note, in each of the 3 cases in this study that presented with diffuse wall thickening, there was a strong clinical history suggestive of malignancy (ie, jaundice, weight loss) that should have pointed toward the correct diagnosis. In each of these cases, the wall was substantially thickened up to an average of 14 mm. Of the 16 patients in this series, 4 were incorrectly diagnosed prospectively, including 1 patient with a discrete polyploid mass (diagnosed with acute cholecystitis), 4 with focal wall thickening, and 1 with diffuse circumferential wall thickening.¹⁸ Most of the polyploid masses in this series were not difficult to diagnose, with a mean size of 37 mm. However, the one case that was not prospectively identified was a small T1 lesion in a patient with acute abdominal pain, no symptoms suggestive of malignancy, and a presumptive diagnosis of cholecystitis. By far, the most common appearance of gallbladder cancer in this series was focal wall thickening (in 9 of the 16 patients), which also accounted for most incorrect prospective diagnoses. Viewed as a group, these tumors were associated with substantial focal wall thickening, extending over an average length of 32.7 mm with an average thickness of 12.2 mm. All 4 of these incorrectly diagnosed cases with focal wall thickening occurred in patients with clinical symptoms of jaundice, and in 3 of the 4 cases, gallbladder thickening was noted, but the focality of this thickening was not appropriately recognized as cancer. Clearly, to arrive at the correct diagnosis, patient symptomatology must be strongly taken into account; moreover, when wall thickening is identified, the thickened wall must be more carefully examined to distinguish a diffusely thickened wall from focal thickening. Nevertheless, given the patients in this series who presented with either no symptoms or symptoms of acute abdominal pain, clinical presentation alone should not be relied upon solely to guide a radiologist's search pattern or to arrive at the correct diagnosis. From the perspective of tumor enhancement, there was a significant variability in the appearance of these tumors in both the arterial and venous phases. Every tumor in this series with dual-phase imaging showed a greater degree of

enhancement on the venous phase images compared with those of the arterial phase, with a mean difference in Hounsfield attenuation between the 2 phases of 28.2 HU. Despite this, there was a dramatic variation in the degree of enhancement between different tumors: A few tumors showed substantial vascularity (HU more than 90 on both the arterial and venous phase images), whereas most cases showed attenuations under 90 HU on both phases. There is little to suggest that the degree of enhancement on either phase of imaging can help make the diagnosis of a malignancy, as opposed to an inflammatory process, and there was certainly no consistent pattern of enhancement across the cases in our series. There are several limitations of our study that should be noted, including the relatively small sample size. The vast majority of gallbladder cancers identified at any institution tend to be unresectable T4 tumors with metastatic disease or bulky locoregional lymphadenopathy. As a result, our study size is small; moreover, most lesions are T3 tumors, with only a few gallbladder-confined T1 and T2 lesions. Nevertheless, given that some T3 tumors are still potentially resectable, these cases stress the critical need for radiologists to identify these T3 tumors while they are still potentially in a resectable state. Second, very few of our patients underwent MRI, limiting our ability to make any definitive statements about the MRI appearance of these tumors. As a result, we have refrained from drawing any strong conclusions about the role of MRI in the evaluation of gallbladder malignancies. Finally, given that not all of our patients underwent dual-phase CT imaging, it would be interesting to look at a larger number of these tumors and gain a better sense of the true enhancement characteristics of these lesions. Gallbladder cancer is associated with extraordinary high mortality and poor clinical outcomes, making it imperative that radiologists correctly identify these lesions in their earliest stages. As the cases in this series illustrate, the imaging findings can be quite subtle, regardless of whether the tumor presents as a discrete mass, focal wall thickening, or circumferential diffuse wall thickening, and radiologists must be aware of the wide range of different possible appearances. Moreover, the vast majority of these patients had clinical symptoms suggestive of an underlying malignancy, and this should precipitate a careful evaluation of the gallbladder in all such cases.

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