CASE REPORT – OPEN ACCESS

International Journal of Surgery Case Reports 51 (2018) 186–189

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.casereports.com

Primary squamous cell carcinoma of the gallbladder: Report of a rare neoplasm from the Eastern Province of Saudi Arabia

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ARTICLE INFO

Article history:
Received 14 June 2018
Received in revised form 14 August 2018
Accepted 25 August 2018

Keywords:
Gallbladder
Carcinoma
Squamous cell

ABSTRACT

INTRODUCTION: Primary squamous cell carcinoma of the gallbladder is extremely rare, and accounts for about 3% of all malignant gallbladder neoplasms.
PRESENTATION OF CASE: We report the case of a 58-year-old woman who presented with acute onset epigastric pain radiating to the back. The initial diagnosis, based on radiological images, was an incidental gallbladder mass with multiple gallstones. A staging laparoscopy was performed, followed by exploratory laparotomy with radical cholecystectomy. Segments 4b and 5 of the liver and the first part of the duodenum with the transverse colon were also resected. Histopathology of the gallbladder mass revealed invasive moderately differentiated squamous cell carcinoma with infiltration of liver segments 4b and 5, the first part of the duodenum, and two pericaval lymph nodes (with lymphovascular and perineural invasion). The primary tumour was scored as pT3, pN2, M1, stage IVB, based on the American Joint Committee on Cancer classification, version 7. The patient was discharged postoperatively and started adjuvant chemotherapy.
DISCUSSION: The best option for treating early-stage gallbladder cancer is radical surgery, while adjuvant chemo-radiation can also be beneficial. Our patient did not exhibit the typical symptoms of gallbladder cancer, and radiography was required for her diagnosis. Thus, additional work is needed to improve the detection of squamous cell carcinoma to improve the prognosis of patients like our own.
CONCLUSION: Clinicians must be alert to the possibility of squamous cell gallbladder carcinoma, and gallbladder neoplasms should be among the possibilities considered during the differential diagnosis of symptoms related to the gallbladder.

1. Introduction

Gallbladder cancer is a rare neoplasm in the Middle East, and is not among the top ten cancers in the Kingdom of Saudi Arabia, according to the Saudi Cancer Registry [1]. Gallbladder cancer is more common in women, and the age at diagnosis is usually greater than 50 years [2]. Squamous cell carcinoma of the gallbladder accounts for about 3% of all gallbladder malignant neoplasms worldwide [3]. In contrast, adenocarcinoma is the most common type of gallbladder carcinoma, and it accounts for the majority (97%) of such cancers [4,5]. Although the silent nature of gallbladder cancer makes it hard to diagnose, recent developments in imaging technologies have enabled early detection [6]. While early clinical presentations can erroneously suggest other conditions, advanced-stage gallbladder cancer usually manifests clinically as abdominal pain, particularly in the upper right quadrant of the abdomen [7]. Rare cases of unusual presentations of gallbladder cancer such as acute cholecystitis, gallbladder empyema, pyoperitoneum, cholecystogastric or cholecystocolic fistulae, liver abscesses, and ruptured gallbladder mucoceles have been reported, and such atypical presentations may be confounding to clinicians. Here we report a rare neoplasm of the gallbladder. Our goal is to shed light on this rare type of gallbladder cancer, and to raise awareness of this cancer in physicians, even if it is rare in our country. This case report is in line with the SCARE criteria [8].

2. Presentation of case

A 58-year-old woman visiteda regional hospital with a 1-month history of moderate epigastric pain radiating to the back, associated with vomiting 4–6 times per day. She was not known to have cholelithiasis. She denied any history of right upper quadrant pain, change in the colour of her urine or stool, or yellowish discoloration of the sclera or skin. There was also no history of decreased appetite or weight loss. At the referral hospital, the patient was diagnosed with acute cholecystitis and cholelithiasis presenting as an acute

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https://doi.org/10.1016/j.ijscr.2018.08.048

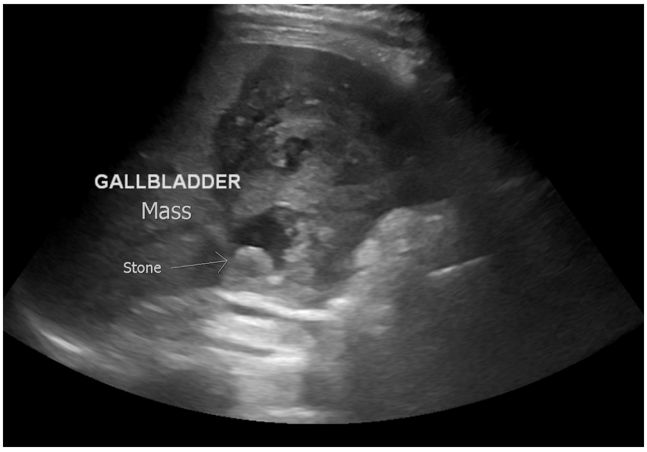

Fig. 1. Abdominal ultrasonography image showing a stone measuring 2.6 cm and an incidental gallbladder mass measuring 6.32 × 5.87 cm with extension to liver segment 5.

episode of biliary pancreatitis, based on clinical, laboratory, and ultrasonographic findings; the presence of a gallbladder mass was not suspected.

The patient was referred to our hospital for an endoscopic retrograde cholangiopancreatography. Two days prior to her outpatient appointment, she presented with severe uncontrolled epigastric pain with many vomiting episodes. Upon physical examination she was in severe pain but without jaundice. She was vitally stable and afebrile. Her abdomen was severely tender with guarding, but there were no physical signs of peritonitis or rigidity. Laboratory investigations showed neither leukocytosis nor neutrophilia. The C-reactive protein level was 1.8 mg/L. Liver function tests showed the following results: albumin, 32 g/L; total protein, 53 g/L; alanine aminotransferase, 364 units/L; aspartate transaminase, 527 units/L, alkaline phosphatase, 364 IU; total bilirubin, 13.4 μmol/L; conjugated bilirubin, 12.20 μmol/L; amylase, 239 units/L, lipase, 136 units/L; and cancer antigen 19-9, 125.01 IU/mL. Other laboratory results were unremarkable. Abdominal ultrasonography revealed a stone measuring 2.6 cm in diameter and an incidental gallbladder mass (Fig. 1).

Based on the incidental finding in the gallbladder, a computed tomography scan of the chest, abdomen, and pelvis was obtained, which revealed a large gallbladder mass measuring 6 × 4 cm with solid and cystic components, suggesting gallbladder cancer. The mass had infiltrated the liver, and there were enlarged portocaval lymph nodes (with the largest node measuring 2.7 × 1.7 cm). In contrast, the pancreas had a normal appearance and the bile ducts were not dilated (Fig. 2A and B). Staging laparoscopy followed by exploratory laparotomy with radical cholecystectomy; resection of segments 4b and 5 of the liver was performed, along with resection of the first part of the duodenum with the transverse colon. Histopathological examination of the gallbladder mass revealed invasive, moderately differentiated squamous cell carcinoma invading all layers of the gallbladder with infiltration to the liver. Metastasis to liver segments 4b and 5, the first part of the duodenum, and two pericaval lymph nodes was also observed (Fig. 3A–D). The transverse colon was free of the tumor. According to the histopathological examination, the patient was diagnosed with gallbladder cancer stage IVB: pT3, pN2, M1. The patient was discharged postoperatively in good condition and referred to the medical oncology department, where she was started on adjuvant chemotherapy. In follow-up visits every 3 months for the last 1 years, all examinations gave negative results for the primary squamous cell carcinoma (Fig. 4A and B).

3. Discussion

Adenocarcinoma is the most common type of gallbladder carcinoma, accounting for about 97% of all such carcinomas, followed by squamous cell carcinoma (approximately 3%); adenosquamous carcinoma of the gallbladder is extremely rare [3–5]. A large proportion of gallbladder carcinoma patients are diagnosed at an advanced stage, implying low diagnostic efficiency [9]. Currently, the only viable option for ensuring a high survival rate in patients with early-stage gallbladder cancer is radical surgery [10]. According to recent studies, adjuvant chemo-radiation is highly beneficial for patients with squamous gallbladder cancer [11]. However, a standard treatment protocol has not yet been defined [12]. Studies indicate that gallbladder carcinoma is the most prevalent malignancy of the biliary tract [13], and exhibits wide geographic as well as ethnic variation worldwide [14]. Squamous cell tumours has the highest rates of proliferation and local invasiveness among gallbladder neoplasms [15]. Squamous cell tumours frequently permeate the liver and the right colic angle [16]. Studies indicate that the rate of growth of the squamous component is twice as fast as that of the adenocarcinomatous component [17], with doubling times of 81 and 166 days, respectively [18]. Though the mechanism by which these tumours spread is yet unclear [19], direct local infiltration with reduced incidence of metastases to the loco-regional lymph nodes has been reported [20]. As observed in the present case, it has been reported that this tumour type tends to grow along the gallbladder fossa, and forms a large infiltrative mass that frequently

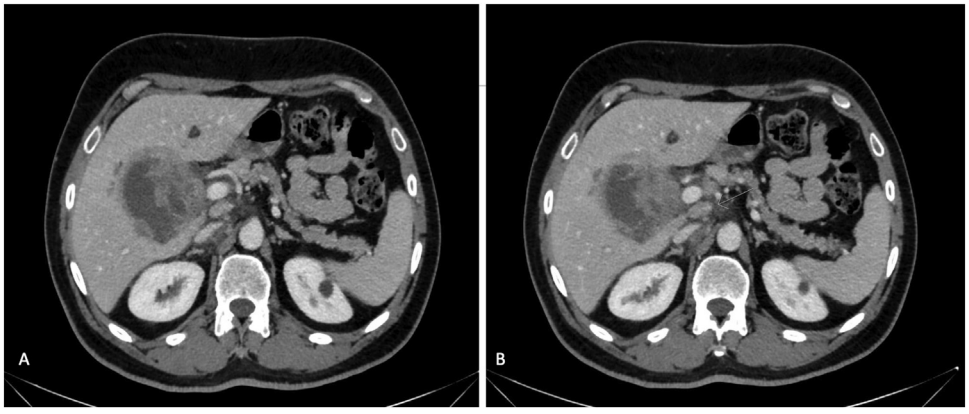

Fig. 2. A and B: A: Computed tomography scan of the chest and the abdomen revealing a large gallbladder mass lesion measuring 6 × 4 cm with solid and cystic components infiltrating the liver. B: Computed tomography scan of the chest and abdomen revealing enlarged portocaval lymph nodes, with the largest node measuring 2.7 × 1.7 cm. In contrast, the pancreas had a normal appearance and the bile ducts were not dilated.