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

Mohammed Y. Aldossary<sup>a,\*</sup>, Amal A. Alayed<sup>a</sup>, Samir Amr<sup>b</sup>, Mohammed S. Alqahtani<sup>a</sup>

<sup>a</sup> Department of General Surgery, Hepatobiliary Unit, King Fahad Specialist Hospital Dammam, Saudi Arabia

<sup>b</sup> Department of Pathology and Laboratory Medicine, King Fahad Specialist Hospital-Dammam, Saudi Arabia

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## 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.

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## 1. Introduction

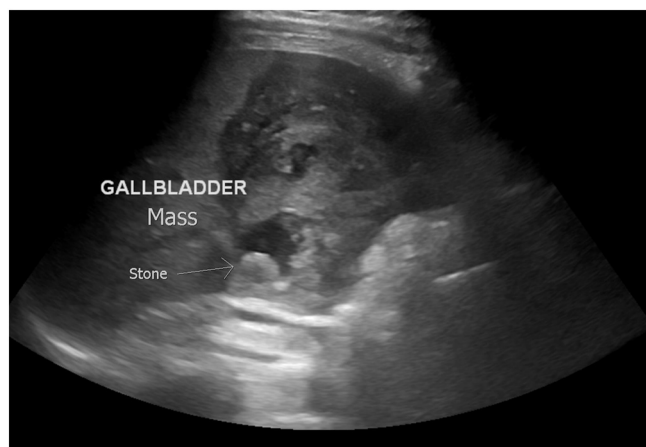
Gallbladder cancer is a rare neoplasm in the Middle East, and is not among the top ten cancers in the Kingdom of Saudi Arabia, according to the Saudi Cancer Registry [1]. Gallbladder cancer is more common in women, and the age at diagnosis is usually greater than 50 years [2]. Squamous cell carcinoma 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 visited a 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

\* Corresponding author at: Department of General Surgery, Hepatobiliary Unit, Building 7, 2nd Floor, King Fahad Specialist Hospital-Dammam, Saudi Arabia.  
E-mail address: [Dr.mohd.Aldossary@gmail.com](mailto:Dr.mohd.Aldossary@gmail.com) (M.Y. Aldossary).



**Fig. 1.** Abdominal ultrasonography image showing a stone measuring 2.6 cm and an incidental gallbladder mass measuring  $6.32 \times 5.87$  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.

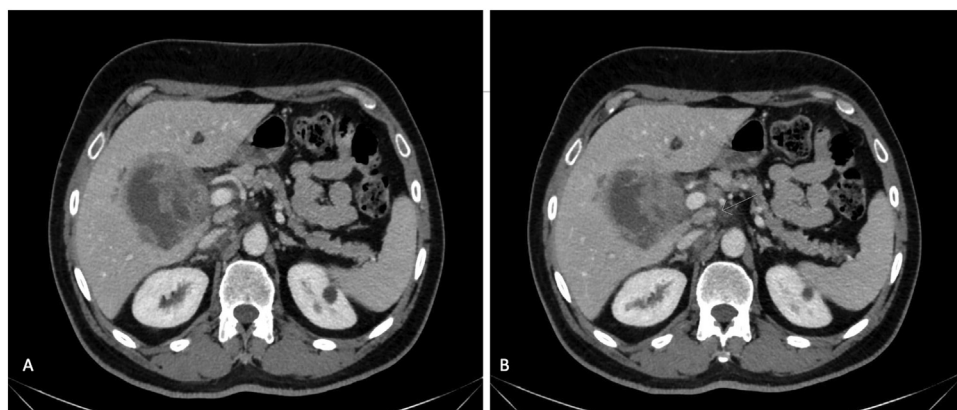
The patient was referred to our hospital for an endoscopic retrograde cholangiopancreatography. Two days prior to her outpatient appointment, she presented with severe uncontrolled epigastric pain with many vomiting episodes. Upon physical examination she was in severe pain but without jaundice. She 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,  $13.4 \mu\text{mol/L}$ ; conjugated bilirubin,  $12.20 \mu\text{mol/L}$ ; 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  $6 \times 4$  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  $2.7 \times 1.7$  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).

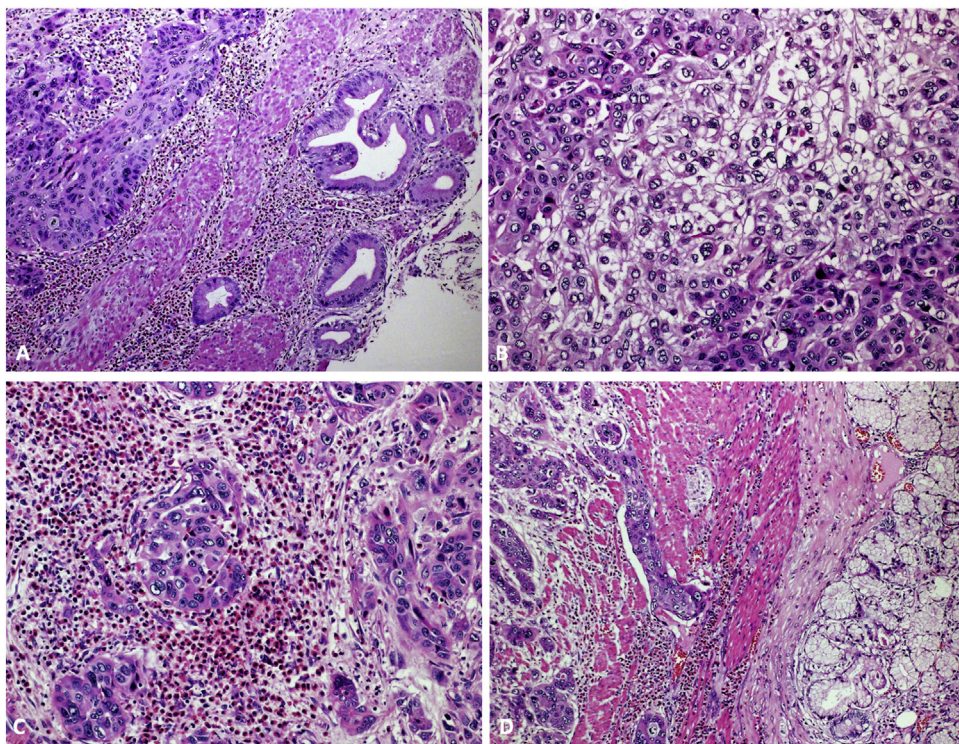
### 3. Discussion

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

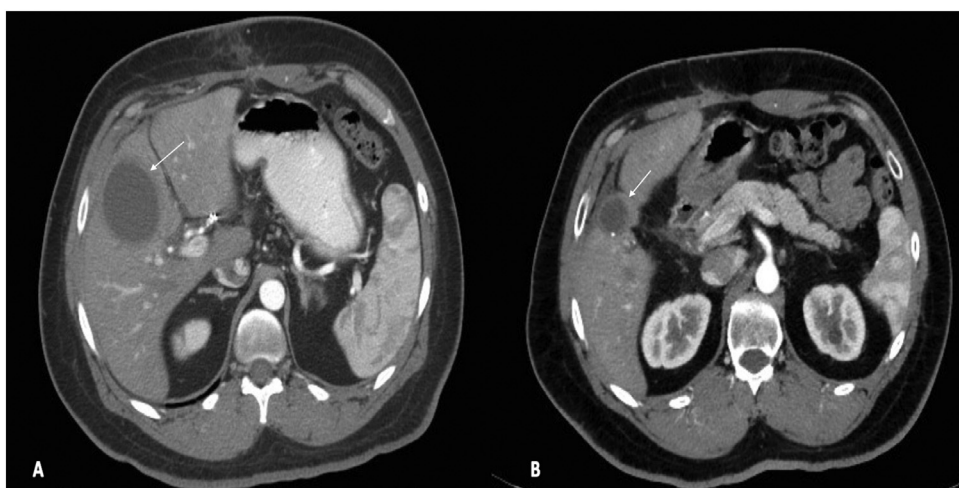


**Fig. 2.** A and B: A: Computed tomography scan of the chest and the abdomen revealing a large gallbladder mass lesion measuring  $6 \times 4$  cm with solid and cystic components infiltrating the liver. B: Computed tomography scan of the chest and abdomen revealing enlarged portocaval lymph nodes,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





**Fig. 3.** A–D: A: Low-power magnification featuring benign gallbladder mucosa and glands with the adjacent muscularis layer, and a solid nest of non-keratinizing squamous cell carcinoma. Tissue eosinophilia is present (H&E  $\times 100$ ). B: Solid sheet of non-keratinizing squamous cell carcinoma with areas of extensive clearing of the cytoplasm due to accumulation of glycogen (H&E  $\times 200$ ). C: Solid nests of high-grade non-keratinizing squamous cell carcinoma with marked tissue eosinophilia (H&E  $\times 200$ ). D: Invasion of the wall of the duodenum by solid nests of non-keratinizing squamous cell carcinoma. Notice clusters of Brenner glands (H&E  $\times 100$ ).



**Fig. 4.** A and B: A: Computed tomography scan of the chest and the abdomen after 3 months post-surgery revealing post cholecystectomy with fluid collection in the gallbladder fossa measures  $5.2 \times 6.8$  cm most likely post-surgical collection, with no suggestion of abdominal and pulmonary metastasis. B: Computed tomography scan of the chest and the abdomen after 9 months post-surgery revealing post cholecystectomy with interval reduction of the surgical site collection measuring 2.5 cm, with no suggestion of abdominal and pulmonary metastasis.

metastasises to the liver and adjacent organs like the duodenum, stomach, and transverse colon [21–23]. The biological behaviour of this tumour is characterized by rapid growth and early metastasis to local and distant regions [24]. Despite the progress made in terms of surgical techniques and adjuvant chemotherapy, the prognosis of squamous cell carcinoma remains poor.

#### 4. Conclusion

In this report, we have described the case of a 58-year-old woman with acute onset epigastric pain radiating to the back. While the initial diagnosis was gallbladder mass and cholelithia-

sis, based on radiological findings, there were a prominent absence of the typical symptoms and signs of acute cholecystitis and malignancy. Given her diagnosis of squamous cell gallbladder carcinoma with atypical symptoms, it is important for clinicians to be alert to this cancer even if it is rare in our country. Accordingly, gallbladder neoplasms should be included in the differential diagnosis of gallbladder-involved symptoms.

#### Conflicts of interest

The authors declare no conflict of interest.

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This study did not receive any funding from governmental or private organizations.

## Ethical approval

Ethical approval was obtained from the Institutional Review Board (IRB) of the King Fahad Specialist Hospital, Dammam, Saudi Arabia. The ethical approval was signed on 25th April 2018.

## Consent

Written informed consent was obtained from the patient for publication of this case report.

## Author contribution

All authors MYD, AAA, SSA, and MSQ participated in Concept, study design, data collection, and Literature search. Writing of the paper were made by MYD and MSQ. All authors read and approved the final manuscript.

## Registration of research studies

None.

## Guarantor

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## Provenance and peer review

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