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Case Report

Gallbladder carcinosarcoma masquerading as a hepatic abscess

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ABSTRACT

Carcinosarcomas of the gallbladder are extremely rare tumors and infrequently reported in the literature. We demonstrate a case of a 64-year-old female who presented with a 2-month history of a right upper quadrant mass, intermittent fevers, and abdominal distension following recent travel to Ghana. A computed tomography (CT) scan of the abdomen and pelvis demonstrated a large hepatic lesion with co-existing gallbladder distension, suggestive of a hepatic abscess. The patient was initially managed with intravenous antibiotics but failed to respond to treatment. A subsequent magnetic resonance imaging (MRI) scan of the liver showed a locally invasive lobulated soft tissue lesion arising from the gallbladder fundus and extending into the liver parenchyma. The lesion was surgically excised with a central hepatectomy. Histopathologic analysis showed a carcinosarcoma of the gallbladder.

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Introduction

Gallbladder carcinosarcomas are highly aggressive tumors associated with a very poor prognosis. These are rare malignancies which are identified by the presence of both mesenchymal and epithelial components on histopathology and fewer than 100 cases are reported in the literature [1–4]. Preoperative diagnosis poses a significant challenge due to a nonspecific and insidious clinical presentation. We report a case of a 64-year-old lady in whom a giant carcinosarcoma of the gallbladder masqueraded clinically as a hepatic abscess. Following the failure of antibiotic treatment and extensive multidisciplinary discussions, she underwent surgical resec-

tion with central hepatic lobectomy and cholecystectomy which revealed her rare diagnosis.

Case report

A 64-year-old female of Afro-Caribbean origin presented with a 2-month history of abdominal pain, distension, intermittent fevers, as well as a noticeable growing lump in the right upper quadrant. She described traveling to Ghana twice in the past year (her last trip was 4 months prior to experiencing symptoms). She denied any history of insect bites or intravenous drug use. Her past medical history included hypertension only,

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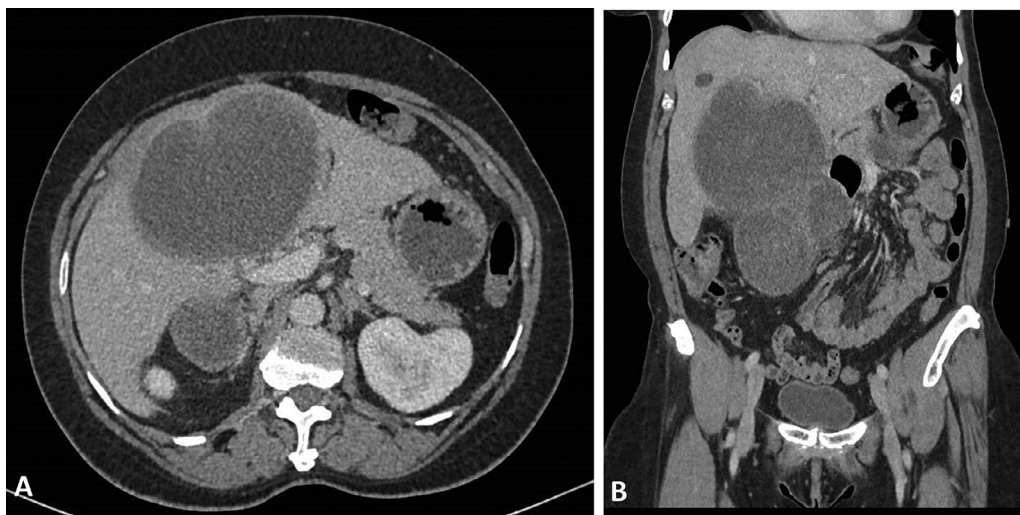


Fig. 1 – (A) Axial CT abdomen and pelvis scan illustrating a giant 12 × 10 × 13 cm hypoattenuated, fluid-filled lesion within the right lobe of the liver. (B) Coronal CT slice showing the hepatic lesion abutting a grossly distended gallbladder. The gallbladder wall is thin and there is no evidence of gallstones or cholecystitis on CT. A single 16-mm cyst is present superolateral to the main hepatic lesion in segment VIII.

for which she was taking amlodipine 5 mg once daily and bendroflumethiazide 2.5 mg once daily. The patient works as a bus driver, denies any smoking history and minimal alcohol consumption (1 glass of wine per week on average).

On examination, a tender mass was palpable in the right upper quadrant with noticeable hepatomegaly. There was no evidence of jaundice, ascites, shifting dullness, or any lymphadenopathy palpable. Cardiovascular, respiratory, and neurologic systems were unremarkable. There was evidence of low-grade pyrexia (temperature 37.9°C) and mild tachycardia (heart rate 108 beats/min); all other vital signs were normal.

Blood tests were in keeping with an inflammatory response of a likely hepatobiliary etiology.

These were as follows: hemoglobin 118 g/L (110-150), white cell count $5.9 \times 10^9/L$ (3.5-11), platelets $462 \times 10^9/L$ (140-400), neutrophils $3.36 \times 10^9/L$ (1.7-7.5), lymphocytes $1.95 \times 10^9/L$

(1.0-4.0), INR 1.1, Na 142 mmol/L (135-145), K 3.9 mmol/L (3.5-5.1), urea 2.7 mmol/L (2.5-7.1), creatinine 54 $\mu\text{mol/L}$ (74-107), bilirubin 13 $\mu\text{mol/L}$ (1.7-20.5), ALT 17 units/L (<50), AST 50 units/L (<50), ALP 129 units/L (50-150), GGT 101 unit/L (9-48), albumin 42 g/L (35-50), and CRP 53 mg/L (0-5). Viral hepatitis, autoimmune hepatitis, and HIV serology screens were negative. Tumor markers showed: alpha-fetoprotein 127.0 kunits/L (0-6), Ca 19-9 7.5 units/mL (0-34), and carcinoembryonic antigen (CEA) 1.1 $\mu\text{g/L}$ (0-4).

A CT abdomen and pelvis with contrast scan performed on admission demonstrated a 12 × 10 × 13 cm low density lesion (fluid attenuation) in the right lobe of the liver with contrast enhancement of the wall, thereby raising the suspicion of a hepatic abscess. On CT imaging, the lesion abutted but appeared to be arising separately from a grossly distended gallbladder with no evidence of cholecystitis (Fig. 1).

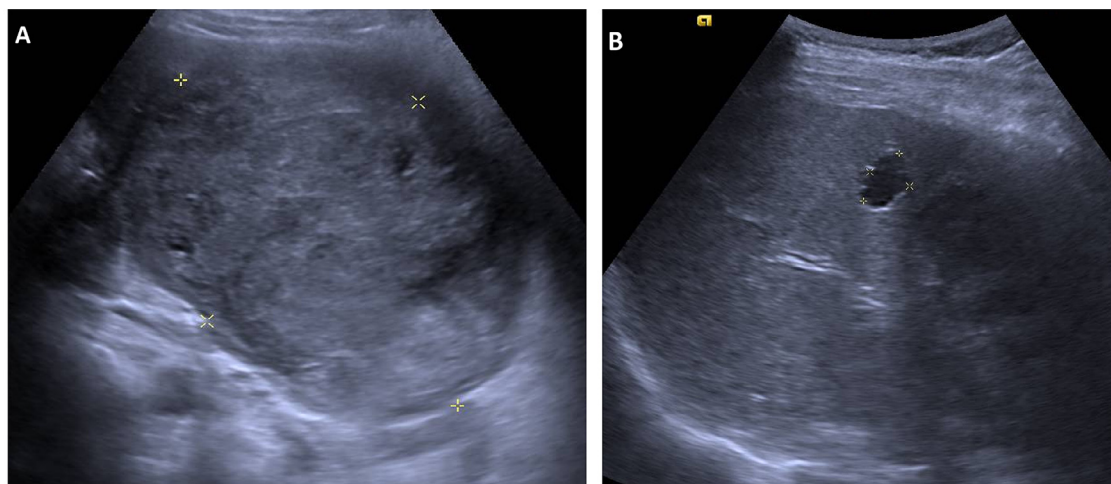


Fig. 2 – (A) Large complex cystic mass in the right lobe of the liver depicted on ultrasound, measuring 132 × 97 × 110 mm. (B) A 16-mm right lobe simple cyst also noted with surrounding coarse architecture of liver and irregular contour.

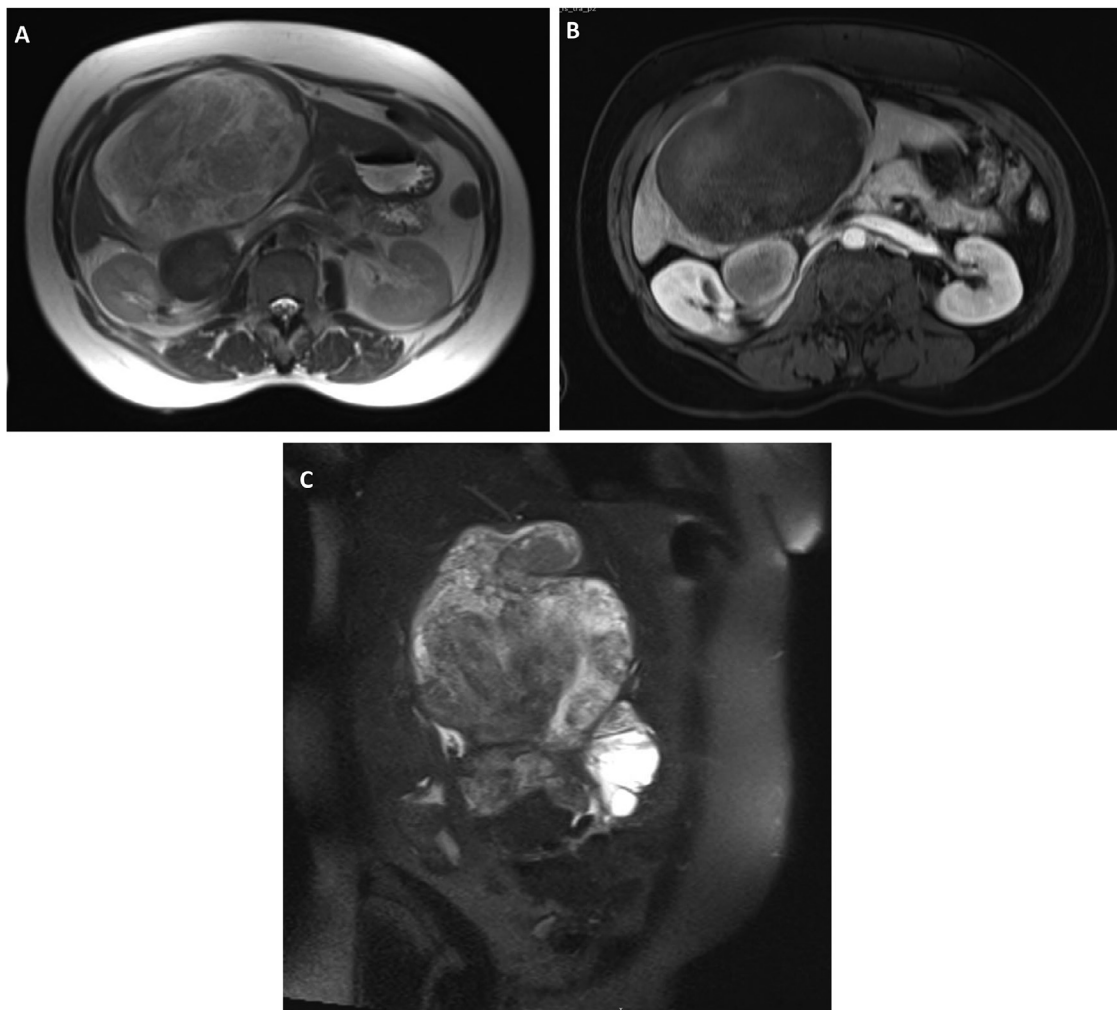


Fig. 3 – Axial MRI slice showing (A) central heterogeneous high T2 signal and (B) low/intermediate T1 signal of a large lobulated soft tissue lesion in the right lobe of the liver. (C) Sagittal MRI T2-weighted sequence illustrating a 5.4 cm × 3.3 cm × 6 cm focus of lobulated enhancing soft tissue arising from the anterior wall of the gallbladder fundus causing gallbladder wall destruction and extending into the liver parenchyma. The origin of the lesion appears to be from the gallbladder, thus raising the suspicion of a gallbladder malignancy with local invasion into the liver.

An ultrasound scan of the liver performed on the following day showed a large complex cystic mass within the right lobe of the liver with no internal vascularity demonstrated on Doppler studies. The gallbladder was unfortunately not identified due to the mass obscuring the field of view; however, the common bile duct and intrahepatic biliary ducts appeared normal. The heterogeneous parenchymal echotexture and partially irregular liver contour was in keeping with chronic liver disease (Fig. 2).

Since the clinical, biochemical, and radiological features were in favor of a hepatic abscess, the patient was treated with a combination of broad spectrum intravenous antibiotics. Unfortunately, she failed to respond to this and continued to experience intermittent pyrexia and her inflammatory markers worsened.

An MRI liver with contrast was performed 1-week after hospital admission. This revealed a 5.4 cm × 3.3 cm × 6 cm

focus of lobulated enhancing soft tissue arising from the anterior wall of the gallbladder fundus with gallbladder wall destruction. There was also a contiguous focus of lobulated soft tissue measuring 12 cm × 9 cm × 14 cm extending into segment 4B of the liver exhibiting central heterogeneous high T2 signal, intermediate T1 signal and peripheral enhancement (Fig. 3). These findings were suspicious for a locally invasive gallbladder malignancy.

The patient was urgently referred to a specialist hepatobiliary surgical unit and underwent surgical resection via a central hepatectomy and a cholecystectomy. Macroscopically, the resected tumor specimen measured 21.5 cm × 13.5 cm × 14.5 cm with a necrotic, hemorrhagic, and cystic appearance. Histopathology demonstrated a biphasic tumor with intramucosal adenocarcinoma and a high-grade spindle cell sarcoma. Within the sarcomatous element, there were areas of chondrosarcomatous differentiation (Fig. 4).

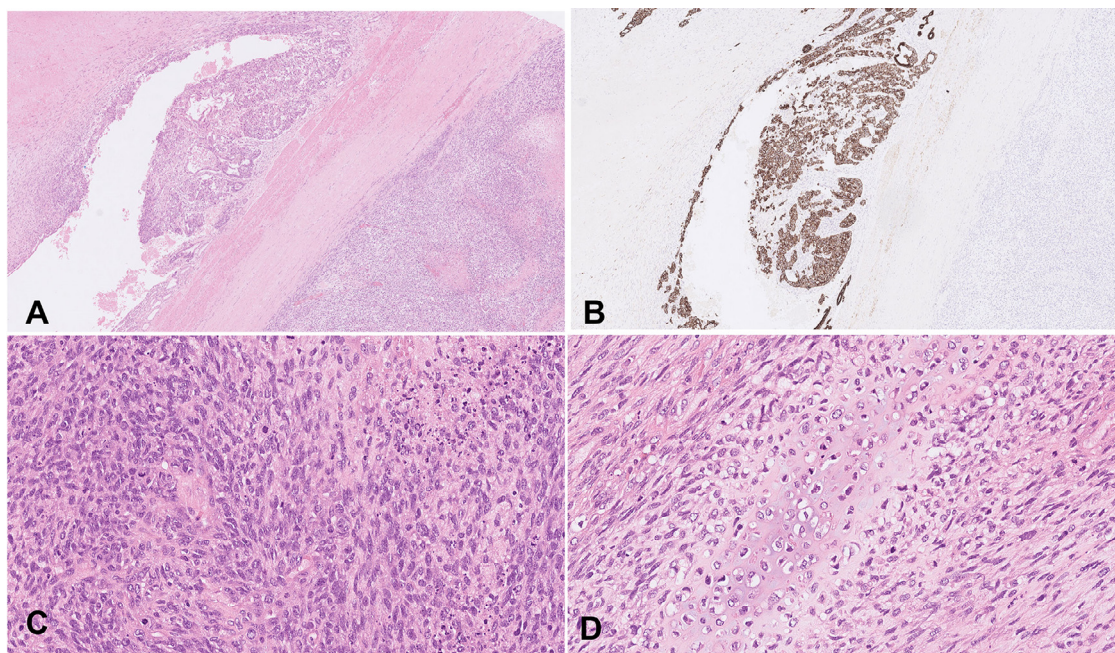


Fig. 4 – (A) Low power view of the gallbladder wall demonstrating showing intramucosal adenocarcinoma and sarcoma (hematoxylin and eosin (H&E) stain, 100 \times). (B) Pan cytokeratin (MNf116, 100 \times) staining showing strong cytoplasmic and membranous positivity in the intramucosal adenocarcinoma. No staining is seen in the sarcomatous component. (C) High power view demonstrating high-grade spindle cell sarcoma (H&E, 800 \times). (D) High power view showing an area of chondrosarcomatous differentiation (H&E, 800 \times).

Discussion

The first reported case of gallbladder carcinosarcoma was in 1907 by Landsteiner et al. [5]. Fewer than 100 cases of gallbladder carcinosarcoma have since been reported in the literature which emphasizes its rarity as a clinical presentation [1]. Adenocarcinoma is the commonest histopathologic type of gallbladder cancer [6]. A diagnosis of carcinosarcoma is made in the presence of 2 distinct histologic components: epithelial and mesenchymal. A meta-analysis by Zhang et al. [7] identified that adenocarcinoma (79.2%) and spindle cell type (44.6%) were the most common epithelial and mesenchymal components respectively. In our case report, these were also these 2 predominant phenotypes with additional foci of chondrosarcomatous differentiation.

The precise mechanism of tumorigenesis of carcinosarcoma of the gallbladder is unknown. It is however postulated that genetic alterations and gene expression patterns are likely to account for sarcomatous changes and epithelial to mesenchymal transition in established cholangiocarcinoma [8]. There are challenges of diagnosing gallbladder carcinosarcoma due to its rarity as well as its vague and insidious clinical presentation for example: weight loss, jaundice, and nonspecific abdominal pain [2]. Additionally, in our presented case, the patient's clinical history, biochemical markers, and preliminary cross-sectional images findings were in keeping with a large hepatic abscess which mas-

queraded the true clinical picture. The lack of response to intravenous antibiotics and suspicious, yet nonspecific MRI findings, helped to identify a malignant process. The initial ultrasound-guided biopsy of the lesion in our case revealed only the sarcomatous component, which further emphasizes the difficulties in diagnosing this condition. Histopathologic and immunohistochemical analysis of resection specimens remains the gold standard of diagnosis.

Surgical management is the mainstay for the treatment of gallbladder carcinosarcoma. For tumors of a smaller size and confinement to the gallbladder, cholecystectomy with excision of involved liver parenchymal margins is preferred. However, large progressive tumors such as in our case report, often receive hemi-hepatectomy and cholecystectomy with lymph node clearance. Despite the intent of curative resection, outcomes are often poor with a 3-year mortality of 31% postresection [9]. In some studies, chemotherapy as adjuvant treatment has been trialed; however, this has not provided any benefit to symptom remission or survival [4,10]. Future studies into new adjuvant oncological treatments are required in an attempt to improve postoperative outcome.

Unfortunately, the prognosis of gallbladder carcinosarcoma is poor with a mean survival being approximately 17.5 months, a 1-year survival rate of 19%, and a 5-year survival rate of 16%. Kaplan-Meier survival analysis in a meta-analysis by Zhang et al. demonstrated that tumor size and ethnicity were independent prognostic factors. Patients who had a tumor size of <5 cm had a significantly longer survival time

(mean of 26.6 months) compared to those with a size >5 cm (17.7 months). Interestingly, Japanese patients also had increased survival time compared to non-Japanese patients. Age, sex, or histologic phenotypes have not been shown to have prognostic value [7].

Consent statement

The authors of this manuscript have obtained written, informed consent from the patient to write up the case report and for the use of images pertinent to the case. We have ensured anonymity of all clinical and graphical data used.

REFERENCES

- [1] Gao S, Huang L, Dai S, Chen D, Dai R, Shan Y. Carcinosarcoma of the gallbladder: a case report and review of the literature. *Int J Clin Exp Pathol* 2015;8(6):7464–9.
- [2] Pu JJ, Wu W. Gallbladder carcinosarcoma. *BMJ Case Rep* 2011;2011(April) bcr0520103009. doi:10.1136/bcr.05.2010.3009.
- [3] Khanna M, Khanna A, Manjari M. Carcinosarcoma of the gallbladder: a case report and review of the literature. *J Clin Diagn Res* 2013;7:560–2.
- [4] Huguet KL, Hughes CB, Hewitt WR. Gallbladder carcinosarcoma: a case report and literature review. *J Gastrointest Surg* 2005;9:818–21.
- [5] Landsteiner K. Plattenepithelkarzinom Und Sarkom Der Gallenblase in Cinem falle von cholelithiasis. *Zischr Klin Med* 1907;62:427–33.
- [6] Kanthan R, Senger JL, Ahmed S, Kanthan SC. Gallbladder cancer in the 21st century. *J Oncol* 2015;2015:967472. doi:10.1155/2015/967472.
- [7] Zhang L, Chen Z, Fukuma M, Lee LY, Wu M. Prognostic significance of race and tumor size in carcinosarcoma of gallbladder: a meta-analysis of 68 cases. *Int J Clin Exp Pathol* 2008;1:75–83.
- [8] Yoo HJ, Yun BR, Kwon JH, et al. Genetic and expression alterations in association with the sarcomatous change of cholangiocarcinoma cells. *Exp Mol Med* 2009;41:102–15. doi:10.3858/emm.2009.41.2.013.
- [9] Okabayashi T, Sun ZL, Montgomey RA, Hanazaki K. Surgical outcome of carcinosarcoma of the gall bladder: a review. *World J Gastroenterol* 2009;15:4877–82. doi:10.3748/wjg.15.4877.
- [10] Liu KH, Yeh TS, Hwang TL, Jan YY, Chen MF. Surgical management of gallbladder sarcomatoid carcinoma. *World J Gastroenterol* 2009;15:1876–9. doi:10.3748/wjg.15.1876.