EAHRC
EAST AFRICAN HEALTH RESEARCH COMMISSION
Research for Health and Prosperity

CASE STUDY

Concomitant Carcinoma of the Gallbladder and Incidental Gallstones, and Concurrent Gallbladder Cyst: A Case Report

Alex Mremi[a,b]*, Mujaheed Suleman[c], Adnan Sadiq[b,d], Jay Lodhia[b,c]

[a]Department of Pathology, Kilimanjaro Christian Medical Centre, Moshi, Tanzania; [b]Faculty of Medicine, Kilimanjaro Christian Medical University College, Moshi, Tanzania; [c]Department of General surgery, Kilimanjaro Christian Medical Centre, Moshi, Tanzania; [d]Department of Radiology, Kilimanjaro Christian Medical Centre, Moshi, Tanzania

Correspondence to Alex Mremi (alex.mremi@kcmuco.ac.tz)

ABSTRACT

Introduction: Gallbladder carcinoma is a malignant epithelial neoplasm of the gallbladder. The tumor is clinically aggressive, with an overall 5-year survival rate of < 10%. Cholelithiasis is a known and established risk factor. Up to 50% of gallbladder tumors are detected incidentally in routine cholecystectomy specimens due to the absence of gross abnormalities. Gallbladder carcinoma has several unusual presentations, one of which is an incidental pseudocyst with cholelithiasis and perforation. This unusual occurrence makes the index case unique.

Case presentation: We report a case of gallbladder cancer diagnosed by an emergency cholecystectomy, performed for acute cholecystitis caused by a pseudocyst. The patient underwent chemotherapy, and currently, 12 months have passed. The patient is doing well, without signs of recurrence or metastasis.

Conclusions: Systematic sampling of cystectomy specimens is therefore crucial to detecting incidental gallbladder adenocarcinomas.

BACKGROUND

Gallbladder carcinoma (GC) is a malignant epithelial tumor with glandular differentiation, arising in the gallbladder.[1] It is a relatively rare and aggressive cancer, with an overall 5 year survival rate of < 10%.[2] The incidence of GC varies in different parts of the world and also differs among different ethnic groups within the same country. In the United States, GC is more common in Native Americans and Hispanic Americans than in whites or blacks.[2] The rate among female Native Americans is 21 per 100,000, compared with 1.4 per 100,000 among white females.[2] In Latin American countries, the highest rates are found in Chile, Mexico, and Bolivia.[3] In Japan, the incidence rates are intermediate.[3] In the general population of the United States, GC accounts for 0.17% of all cancers in males and 0.49% in females. There are limited data on the epidemiology of GC in sub-Saharan Africa. In 2022, the incidence and mortality of GC in Tanzania were estimated at 133 and 97 per 100,000 people respectively.[4]

Primarily, GC is a disease of older age groups. Most patients are in their 6th or 7th decades of life.[2] The incidence of GC is higher in patients with gallstones (cholelithiasis) than in patients without stones; and cholelithiasis is thought to be a major risk factor.[5] Gallstones are present in over 80% of GCs. The incidence of GC parallels that of gallstones, being more frequent in females and in certain ethnic groups, e.g. Native Americans, who have a high incidence of stones. Although gallstones are considered a risk factor, the overall incidence of GC in patients with cholelithiasis is less than 0.2%; this percentage varies with race, sex, and length of exposure to the stones.[6] similarly, abnormal choledochopancreatic junction, porcelain gallbladder, chronic cholecystitis, and genetic susceptibility have been associated with an increased risk.[6]

Usually, GC lesions present late in the course of the disease. The signs and symptoms are not specific, often resembling those of chronic cholecystitis. Right upper quadrant (RUQ) pain is a common clinical presentation.[4] Some patients may present with weight loss and fever, and the disease is usually advanced by the time the patient develops symptoms.[7] Up to 50% of GC is diagnosed incidentally in routine cholecystectomy specimens due to the absence of gross abnormalities.[3] Thus, finding a thickened gallbladder wall or polypoid lesions in the gallbladder on imaging done for other reasons should prompt surgical resection. Cholecystectomy surgery with a negative cystic duct margin is curative in patients with early-stage tumors. Chemotherapy or radiation therapy are reserved for patients with advanced-stages diseases, including metastatic tumors.[8]

Herein, we report a case of gallbladder carcinoma incidentally found in cholecystectomy due to cholelithiasis. A brief review of the literature is also provided.

Ethical consideration

Written informed consent was obtained from the patient for publication for this case report; additionally, accompanying images have been censored to ensure that the patient cannot be identified. A copy of the consent is available on record. A waiver for ethical approval was obtained from the authors' institution review board committee.

CASE PRESENTATION

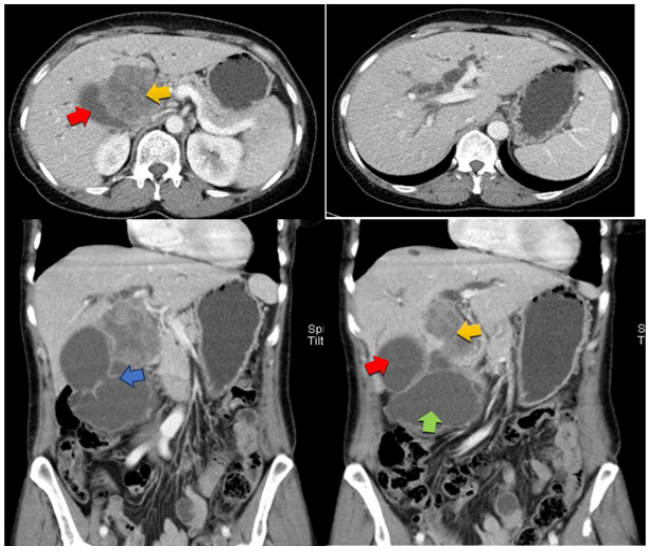
A 61-year-old female patient presented to the surgical outpatient clinic of the Kilimanjaro Christian Medical Centre (KCMC) with a 2-month history of right upper quadrant abdominal pain, sharp in nature, radiating to her right lower abdomen. KCMC is a referral and tertiary hospital located in Kilimanjaro Region of Tanzania. KCMC has over a 750-bed capacity, attending to thousands of patients on a daily basis. The hospital offers both general and specialized care, including surgical gastroenterology and oncology. KCMC is also a university teaching hospital for Kilimanjaro Christian Medical University College.[9] As a zonal hospital, KCMC caters for over 15 million people in five regions of northern Tanzania, namely Kilimanjaro, Arusha, Tanga, Singida, and Manyara. The patient described her pain as associated with yellowish discoloration of the eyes, which was progressively increasing over time. She was passing deep yellow urine and pale stools. She also reported a history of nausea and vomiting from recently eaten food material, and weight loss of about 5 kg over the past two months. Abdominal ultrasound revealed features of cholelithiasis and an intra-abdominal mass measuring 4.5 x 5.8cm.

Upon admission, she was alert, not pale, and not jaundiced, with a blood pressure of 112/73 mmHg, a pulse rate of 88 beats per minute, a respiratory rate of 22 breaths per minute, an oxygen saturation pressure (SPO_2) of 96% on room air, and a temperature of 37.1°C. She had bilateral pitting lower limb edema. Her abdominal examination revealed symmetrical contours, moving with respiration, no surgical scars, guarding on palpation over the right upper quadrant and tenderness over the right lower quadrant, no organomegally noted and normal bowel sounds. Other systems were essentially normal.

Her abdominal computed tomography (CT) scan revealed a multi-lobulated mass arising from the periportal region measuring 7 x 7.1 x 7.7 cm in size. The mass was abutting the gallbladder and compressing the common hepatic duct at the confluence. There was moderate upstream intra-hepatic biliary dilatation. Features were suggestive of moderate biliary obstruction secondary to periductal cholangiocarinoma versus cholelithiasis. A multilobulated, thin-walled cystic lesion was seen inferior to the periportal mass and communicated with the gallbladder, measuring 6.2 x 9.4 x 14.3 cm in size. Features suggestive of a contained perforation of the gallbladder were considered. The gallbladder was adequately distended with multiple calculi, the largest measuring 1.2 cm in size. The liver size was normal, with severely dilated intrahepatic biliary radicles (Figure 1). Her chest x-ray was essentially normal.

Her blood analysis had an elevated leucocyte count of 19.65 x 10^9/L, predominantly neutrophils of 87.5%, microcytic normochromic anemia with hemoglobin of 10.5g/dl, and a platelet count of 415 x 10^9/L. Her liver function test revealed elevated aspartate aminotransferase (AST) of 319U/L, alanine transaminase (ALT) of 205U/L, total bilirubin of 578.7 µmol/L, conjugated bilirubin of 212.50 µmol/L. Her serum creatinine was 108 µmol/L and her blood urea nitrogen (BUN) was 11.08 mmol/L. Her albumin level was 29.4 g/L. Alphafeto protein was 4.65 IU/L and the blood group was O, rhesus-positive.

FIGURE 1: CT-scan Axial and Sagittal Images of the Abdomen Showing a Multi-lobulated Gall Bladder Mass



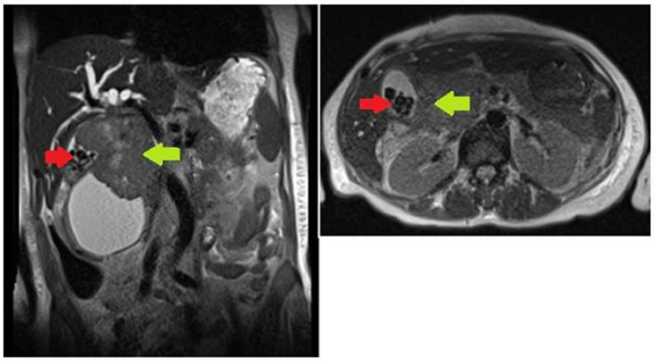
CT-scan axial and sagittal images of the abdomen showing a multi-lobulated gall bladder mass (yellow arrow) compressing the common hepatic duct at the confluence. There is moderate upstream intrahepatic biliary dilatation. A thin-walled cystic lesion seen inferior to the gall bladder mass and communicates with the gall bladder (blue arrow) suggestive of contained perforation of the gall bladder (green arrow).

A magnetic resonance cholangiopancreatography (MRCP) was also done, which revealed a well-defined mixed-signaled mass with a large inferior cystic component in the periportal region measuring approximately 7.7 x 8.7 x 15 cm in size. A periportal mass compresses the common hepatic duct and the common bile duct (CBD), with infiltration of the gallbladder. Features were suggestive of periductal GC (Figure 2).

She was scheduled for a laparotomy, which revealed a cyst attached to the gallbladder on the inferior aspect with multiple stones (Figure 3). There was another mass around the proximal CBD with periportal lymphadenopathy. The gallbladder cyst was deroofed, gallstones extracted, and specimens were taken from the cyst wall, gallbladder, lymph node, and CBD mass for histopathological evaluation. A subcutaneous drain was placed into the cyst to drain the bile and relieve her jaundice. Post-operatively, her jaundice reduced clinically, and laboratory investigations were done, which revealed

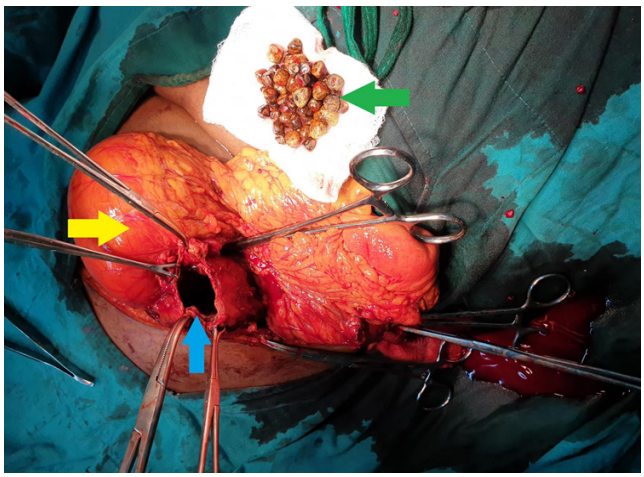
a conjugated bilirubin of 190.5 µmol/L, a total bilirubin of 505 µmols/L, a serum urea of 10.41 mmol/L and a creatinine of 47 µmol/L. Histopathology results of the biopsy revealed an infiltrative tumor made up of glandular structures of a papillary pattern with positive surgical margins, consistent with invasive adenocarcinoma (Figure 4). The lymph node was negative for the tumor.

FIGURE 2: MRCP Coronal and Axial View Shows Similar findings to Abdomen CT Scan



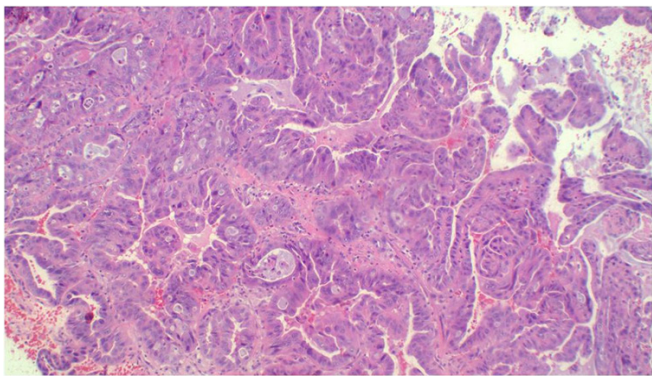
MRCP coronal and axial view shows similar findings to abdomen CT scan (periductal gallbladder carcinoma – green arrow), however, multiple calculi seen in the gall bladder suggestive of cholelithiasis (red arrow).

FIGURE 3: Retracted Gallbladder



Retracted gallbladder (yellow arrow) communicating with cyst (blue arrow) containing gallstones (green arrow)

FIGURE 4: Histopathology Highlighting an Invasive Gallbladder Carcinoma



Histopathology highlighting an invasive gallbladder carcinoma made up of atypical glandular structures, H&E staining 100X original magnification

She was then discharged and instructed to attend the out-patient clinic after 4 weeks. A new panel of blood workup was taken during her visit to our out-patient clinic which revealed a total bilirubin of 513.9µmol/L, conjugated bilirubin of 458.60µmol/L, serum sodium of 128.30mmol/L, serum potassium of 3.54 mmol/L, gamma-glutamyltransferase of 750.90U/L, elevated aspartate aminotransferase (AST) of 297.80U/L, alanine transaminase (ALT) of 76.30U/L. Her complete blood count (CBC) revealed an elevated leucocyte count of 23.45x10^9/L predominantly of neutrophils of 90.1%, microcytic normochromic anemia with HB of 10.3g/dl and a normal platelet count of 424x10^9/L. She finished chemotherapy 12 months ago, and currently she is under surveillance.

DISCUSSION

Gallbladder carcinoma (GC) is a dangerous malignant tumor of the biliary tree that is often diagnosed very late, giving it a poor prognosis.[1,2,3] The lack of screening tests for early tumor detection and the tumor's aggressive nature are the main causes of the poor prognosis. It is responsible for 165,000 cancer deaths each year, or 1.7% of all cancer deaths worldwide. GC is the 22nd most common and 17th most lethal carcinoma globally, according to GLOBOCAN 2022 data.[4] The incidence accounts for 1.2% of all cancer diagnoses globally, with females (122,000) experiencing the disease at a higher rate than males (97,000). Eastern Europe, East Asia, and Latin America have the highest incidence rates.[3] However, in Africa, a few cases of GC have been reported; most are diagnosed incidentally from the histopathology of cholecystectomy specimens after surgery for presumed symptomatic cholelithiasis.[5]

Despite being the most common malignancy of the biliary tree and the third most common cancer of the gastrointestinal tract, GC remains a rare neoplasm that displays notable geographic variability. It is the fifth most common neoplasm of the gastrointestinal tract and the most common cancer of the biliary tract.[6] GC is suspected

preoperatively in only 30% to 40% of patients. As was in the index case, most GCs that account for 60% to 70% rate are discovered incidentally by the pathologist on a gallbladder specimen following cholecystectomy for benign diseases such as polyps, gallstones, and cholecystitis. GC is relatively less prevalent in developed countries like Australia, displaying an approximate incidence of 1.4 cases per 100,000 population. GB cancer has a high mortality rate, which is attributed to the nonspecific features of the disease, the frequent advanced stage at the time of diagnosis, and the significance of organs in proximity to the gallbladder's position. Presently, the only curative management of disease is surgical, requiring microscopically margin-negative resection (R0 resection) of disease before peripheral spread has had the opportunity to occur.[7]

Many authors have described various GC disease manifestations, such as empyema, cholecystitis, biliary stricture, liver abscess, gastric outlet obstruction, and tumors of the head of the pancreas.[5] Similar symptoms include stomach pain, nauseousness, vomiting, and jaundice.[6] Anorexia (35%), weight loss (35%), nausea and vomiting (43%), jaundice (37%), and abdominal pain (73%), according to Singh et al.[8] Ascites, a palpable mass, and constitutional symptoms are all signs of an advanced illness with a poor prognosis. Ascites, the presence of supraclavicular lymph nodes, and skin nodules were also found. Regarding our case, it is obvious that it is a rare presentation seen in clinical and surgical practice to have a large cystic component containing gallstones in a GC that is worth discussing. The gallbladder perforation that led to the cystic component's development may have been concealed.[10] Since our patient is female, the cyst's association with gallstones is most likely one of its actual contents. Emphesematous cholecystitis and pancreatitis, the development of a cholecystocutenous fistula, and necrotizing fasciitis with gallbladder perforation are additional uncommon and distinct presentations seen in patients with GC.[8,11,12,13]

Unusual gallbladder perforations have been the subject of several published case reports. For instance, a case report written by Suleiman et al, described an 82-year-old woman who had a concealed gallbladder perforation secondary to cholecystitis and displayed a clinical picture similar to ours.[12] Another study by Kim et al, (2004) discussed the case of a 70-year-old woman who had an acute abdomen and was later diagnosed with peritonitis brought on by a spontaneous gallbladder perforation, despite the absence of any symptoms suggestive of this condition. Although uncommon and rare, this case demonstrates that this disorder should be taken into account in elderly patients who present with peritonitis of unknown origin.[14] Other unusual cases published on gallbladder perforations include gallbladder perforation due to enteric fever, in which a 20-year-old male presented with features of anacute abdomen with a positive typhoid test and intra-operative findings of multiple perforations of the gallbladder, and perforation due to isolated gallbladder tuberculosis.[15,16]

A potential caveat in our case is the limited access to comprehensive molecular diagnostic tests that are currently not feasible in our setting. For instance, we were not able to perform molecular and cytogenetic studies to describe the common GC genetic alterations, including *TP53*, *CDKN2A*, *ARID1A*, *PIK3CA*, and *CTNNB1*. Similarly, due to limited resources, tests for ERBB2 (HER2), MSI, and KRAS determination are not feasible in our setting.

CONCLUSION

In conclusion, incidental carcinoma of the gallbladder, as our experience confirms, is generally diagnosed at an earlier stage and carries a better prognosis than non-incidentally found cancer. Gallbladder carcinoma continues to be an aggressive and relatively uncommon cancer with a wide range of clinical manifestations. It has the worst overall prognosis of any biliary tract malignancy (5 year survival rate of only 10%). Cholelithiasis is a recognized and significant risk factor. Due to the absence of obvious abnormalities, up to 50% of gallbladder carcinoma cases are discovered incidentally in routine cholecystectomy specimens. The disease might unintentionally have been discovered earlier with a laparoscope. Therefore, it is essential to thoroughly and methodically sample resection specimens in order to find incidental gallbladder carcinomas.

REFERENCES

1. Wernberg JA, Lucarelli DD. Gallbladder cancer. Surg Clin North Am. 2014;94(2):343-60. doi: 10.1016/j.suc.2014.01.009.
2. Schmidt MA, Marcano-Bonilla L, Roberts LR. Gallbladder cancer: epidemiology and genetic risk associations. Chin Clin Oncol. 2019;8(4):31. doi: 10.21037/cco.2019.08.13.
3. Okaniwa S, Fujita N, Noda Y, et al. [A clinico-pathological study of early gallbladder carcinoma]. Nihon Shokakibyo Gakkai Zasshi. 1996 Sep;93(9):628-33. Japanese.
4. Global Cancer Observatory: Cancer today. Lyon, France: International Agency for Research on Cancer. Population factsheet. Available from https://gco.iarc.who.int/media/globocan/factsheets/populations/834-tanzania-united-republic-of-fact-sheet.pdf Accessed 20 04 2024
5. Rawla P, Sunkara T, Thandra KC, Barsouk A. Epidemiology of gallbladder cancer. Clin Exp Hepatol. 2019;5(2):93-102. doi: 10.5114/ceh.2019.85166.
6. Khan ZA, Brand M. Incidental gallbladder cancer–the first report from Africa. HPB. 2019;21 (Suppl: 3):S549. https://doi.org/10.1016/j.hpb.2019.10.103
7. Kumar R, Gupta N, Dey P, Chaluvashetty SB, Gorsi U. An unusual presentation of carcinoma in gallbladder. Cytojournal. 2019;16:3. doi: 10.4103/cytojournal.cytojournal_15_18.
8. Singh SK, Talwar R, Kannan N, Tyagi AK, Jaiswal P, Kumar A. Patterns of Presentation, Treatment, and Survival Rates of Gallbladder Cancer: a Prospective Study at a Tertiary Care Centre. J Gastrointest Cancer. 2018;49(3):268-274. doi: 10.1007/s12029-017-9940-y.
9. Kilimanjaro Christian Medical Centre. kcmc.ac.tz
10. Matsumoto M, Maruta M, Maeda K, Utsumi T, Sugioka A, Kuroda M. Epithelial cyst of the gallbladder associated with adenocarcinoma. J Hepatobiliary Pancreat Surg. 2002;9(3):389-92. doi: 10.1007/s005340200047.

11. Serrano, PU, Garcia LS, de Leon AM, Arrillaga IG, Gonzalez JG. [Cholecystocutaneous Fistula as a First Sign of Presentation of a Gallbladder

Adenocarcinoma]. Cir Esp. 2013;91:396–397. Spanish.

12. Okada KI, Shatari T, Yamamoto T, et al. Necrotizing fasciitis secondary to carcinoma of the gallbladder with perforation. Journal of Hepato-Biliary-Pancreatic Surgery. 2007;14(3):336-9.

13. Suleiman J, Mremi A, Tarmohamed M, Sadiq A, Lodhia J. Concealed gallbladder perforation: a rare case report. Journal of Surgical Case Reports. 2021;2021(6):rjab245.

14. Kim HJ, Park SJ, Lee SB, et al. A case of spontaneous gallbladder perforation. Korean J Intern Med. 2004;19(2):128-31. doi: 10.3904/kjim.2004.19.2.128.

15. Malik MN, Mahmood T, Tameez Ud Din A, Aslam S, Imtiaz M. Gallbladder Perforation Secondary to Enteric Fever: An Interesting Case of Acute Abdomen. Cureus. 2019;11(4):e4516. doi: 10.7759/cureus.4516.

16. Tarmohamed M, Mremi A, Mkwizu E, Paschal J, Sadiq A, Msuya D. Isolated gallbladder tuberculosis in an 84-year old man: A rare case report. Int J Surg Case Rep. 2021;87:106471. doi: 10.1016/j.ijscr.2021.106471.

Peer Reviewed

Acknowledgements: The authors would like to thank the staff in the General Surgery and Pathology Departments including Ummil J. Koosa and Daniel Mbwambo for supporting this study as well as the patient for allowing us to use his medical information for academic purposes.

Competing Interests: None declared.

Funding: The study did not receive any funding.

Received: 18 February 2024; **Accepted:** 13 March 2024

Cite this article as Mremi A, Suleman M, Sadiq A, Lodhia J. Concomitant Carcinoma of the Gallbladder and Incidental Gallstones, and Concurrent Gallbladder Cyst: A Case Report. East Afr Science J. 2024: 6(1): 10-14. https://doi.org/10.24248/easci.v6i1.87