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Case report

Challenges in diagnosing and managing cystic duct carcinoma: A case report from Syria

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ABSTRACT

Introduction and importance: Primary cystic duct carcinoma, an uncommon and aggressive biliary cancer variant, poses a significant challenge in clinical practice. This study examines recent clinical cases, focusing on diagnostics, interventions, and implications in managing this disease, with a prevalence ranging from 0.03 % to 0.05 %, contributing to 2.6–12.6 % of extrahepatic biliary neoplasms.

Case presentation: A 57-year-old male, a smoker with hypertension and hyperuricemia, presented symptoms of severe upper right abdominal pain, jaundice, and altered stool color. Diagnosis revealed ulcerated papillary adenocarcinoma invading all gallbladder layers (2.5 cm). Surgical resection and Roux-en-Y anastomosis were performed. Histopathological examination showed invasive tumor proliferation, preserved lymph node architecture, and severe hepatic microsteatosis. Lymph nodes were tumor-free, and a benign hepatic biopsy (0.5 cm) displayed chronic portitis. The final diagnosis confirmed cystic duct carcinoma, emphasizing the complex diagnostic and therapeutic aspects in biliary cases.

Clinical discussion: The clinical discussion unveils the complexities associated with primary cystic duct carcinomas. Emphasizing the necessity of a multidisciplinary approach, this case highlights the importance of efficient management strategies—from initial diagnosis to surgical intervention—in dealing with this challenging malignancy.

Conclusion: In conclusion, this case underscores the intricate nature of primary cystic duct carcinomas. It accentuates the essential role of a multidisciplinary approach, urging the need for continuous research endeavors to further comprehend and enhance the treatment methodologies for this rare and complex malignancy.

1. Introduction

The field of oncology is witnessing the emergence of a unique entity, carcinoma of the cystic duct, which is a rare and aggressive cancer variant within the biliary system. The propensity for localized invasion and extensive metastasis requires rigorous investigation. This analysis comprehensively examined recent clinical cases, addressing diagnostic challenges, strategic interventions, and clinical implications.

Primary cystic duct carcinoma is a rare type of cancer that arises within a narrow range of prevalence (0.03–0.05 %) and holds a significant position among extrahepatic biliary neoplasms (2.6–12.6 % incidence), as determined by Farrar's diagnostic criteria [1–3]. Gastrointestinal malignancies reveal extrahepatic biliary duct pathologies (2–3.6 % incidence), where primary cystic duct carcinoma arises as an enigmatic entity, documented in fewer than 70 cases worldwide since 2017 [4]. With a preference in East Asia and scarcity in the Indian subcontinent, we present a case of laparoscopic cholecystectomy [4]. Earlier classification by Farrar [3] lacks synchrony due to rigidity. Contemporary paradigms rectify limitations and illuminate complex biological behavior in this formidable neoplasm [5,6]. This work has

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been reported in line with the SCARE criteria 2023 [7]. We present the case of a 57-year-old man who was experienced jaundice and severe pain in the upper right abdomen. The patient was diagnosed as having cystic duct cancer.

2. Case presentation

A 57-year-old married male smoker with hypertension and hyperuricemia, taking colchicine and antihypertensives, reported severe upper right abdominal pain, unchanged by painkillers, for three days to a small emergency department. Accompanying symptoms included nausea, altered stool color, but no fever, diarrhea, constipation, appetite loss, or other symptoms. The patient was alert, responsive, and oriented; vital signs were normal. Jaundice was seen in the sclera and mucous membranes, with mild tenderness in the right hypochondrium and a soft, non-distended abdomen. The other systems were normal. Emergency lab tests showed extremely high ALT (926 IU/L), amylase (139 U/L), and LDH (HIGH U/L). Subsequently, an ultrasound (Fig. 1) was performed, which showed severe inflammatory stones without dilation of the intrahepatic bile ducts (IHBR) or common hepatic duct. The patient experienced acute pancreatitis resulting from acute cholecystitis, accompanied by choluria. They were transferred for emergency ERCP and cholecystectomy and given anti-emetics, proton pump inhibitors, and painkillers as a precaution. They were then transferred to a specialized hospital. Laboratory tests were conducted upon admission to a specialized hospital. The white blood cell count, amylase, and lipase levels were within normal limits, but the total bilirubin levels were significantly elevated at 5 mg/dL, direct bilirubin at 4 mg/dL, ALT at 697 IU/L, AST at 886 IU/L, and tumor marker Ca19–9 at 70.1 U/mL.

3. Radiological investigation

During ERCP, bloody bile was observed. A biopsy specimen was taken from the sphincter of Oddi, a balloon was inserted to drain the blood sludge from the collecting duct, and a plastic stent was placed to maintain duct patency. A contrast-enhanced CT scan (Fig. 2) revealed the plastic stent in the left hepatic duct, a distended gallbladder without stones or thickening, and no contrast leakage or hematoma. A 1.6 cm lesion in the spleen, enhanced during the venous phase, was consistent with a hemangioma. Post-MRCP (Fig. 3), a stent was seen in the common bile duct, and a distended gallbladder with 11 × 5 cm sludge and possible neck mass of 1.6 × 1.4 cm was identified. Two more masses (1.6 × 1.4 cm and 1 × 1 cm) in the spleen resembled hemangiomas. A 1 cm cyst was found in the left kidney. After undergoing MRI (Fig. 4), the splenic lesion showed enhancement during the injection phase. Subsequently, a contrast-enhanced CT scan of the chest was performed, which showed several nodules at the lung base, with the largest measuring 5 mm on the left, without any evidence of cavitation.

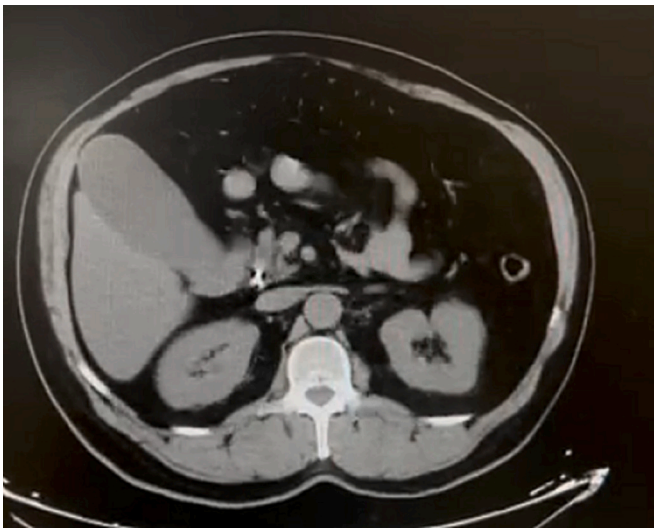

Fig. 2. A contrast-enhanced CT scan revealed the plastic stent in the left hepatic duct, a distended gallbladder without stones or thickening, and no contrast leakage or hematoma.

Laboratory tests showed white blood cells, red blood cells, platelets, PT, INR, ALT, AST, ALP, amylase, total bilirubin, direct bilirubin, creatinine, urea, and glucose were all normal. The patient's hemoglobin, hematocrit, MCV, MCH, MCHC, ALP, Na, and K were all above normal

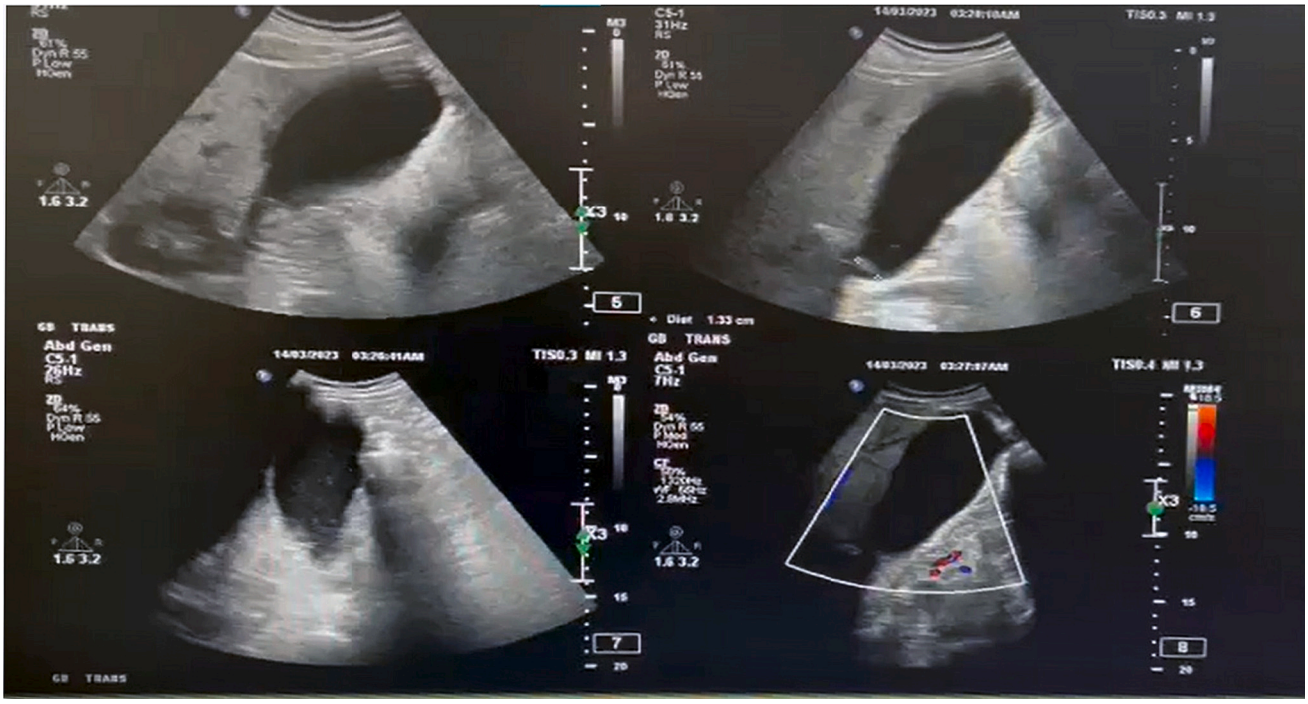

Fig. 1. Ultrasound shows severe inflammatory stones without dilation of the intrahepatic bile ducts (IHBR) or common hepatic duct.

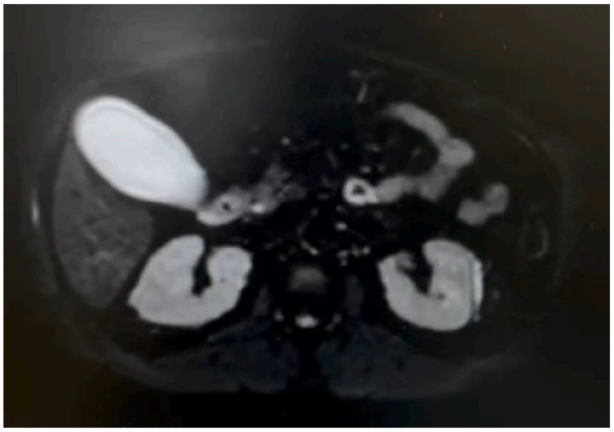

Fig. 3. MRCP shows a stent was seen in the common bile duct, and a distended gallbladder with 11 × 5 cm sludge and possible neck mass of 1.6 × 1.4 cm was identified.

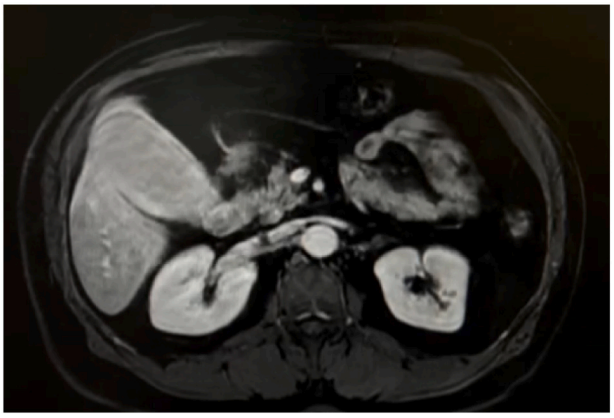

Fig. 4. MRI shows the splenic lesion showed enhancement during the injection phase.

levels (9.7 g/dL, 30.7 %, 63.56 fl, 20.08 pg/cell, 31.6 g/dL, 3.5 g/dL, 133.3 mmol/L, 3.26 mmol/L). Abdominal and pelvic CT with contrast showed a small hiatal hernia below the esophagus. Mild gallbladder distension (11 × 5 cm) was seen without wall thickening or inflammation. No enhanced mass lesions were seen in the gallbladder. A 1.5 × 2.2 cm enlarged lymph node in the porta hepatis, likely reactive due to prior hepatitis, was seen. A 2.2 cm enhancing lesion in the spleen was consistent with a benign cavernous hemangioma. A stent placed in the common bile duct had migrated to the intestine without obstruction, and was seen in the third and fourth segments of the duodenum. A small left inguinal hernia with fatty tissue and a 1.2 cm calcification in the Douglas pouch were seen. All other results were normal.

Surgical intervention encompassed layered abdominal access, revealing no evidence of metastases or peritoneal involvement. A Kocher maneuver was performed, followed by meticulous isolation of the cystic duct and the entire extent of the common bile duct. The localized mass was identified at the terminal segment of the cystic duct in proximity to its convergence with the common bile duct. Gallbladder resection and removal of the cystic duct ensued, securing a substantial safety margin (approximately 1.5 cm). Notably, the procedure encompassed excision of the cystic duct orifice where it merged with the common bile duct. Closure of the main biliary pathway's root was achieved. Employing the Roux-en-Y technique, a biliary-jejunostomy was executed between the residual portion of the common bile duct and a jejunal loop. Subsequently, a jejunostomy was established. The surgical sequence was concluded with wound closure and bandaging. In our case, we conducted follow-up assessments at three and six months, during which we observed a marked and substantial improvement in the patient's overall condition.

4. Histopathology

Histopathological analysis of the obtained specimens revealed significant insights into the case. The gallbladder specimen, measuring 13 × 4 cm, with a thick wall of up to 2 cm, contained a 2.5 cm ductal (cystic duct) fungating mass, appearing white and firm upon cutting. Microscopic examination unveiled ulceration and severe chronic inflammatory infiltrates permeating all layers of the wall. Notably, tumoral proliferation characterized by papillae, tubules, and glands lined by large polygonal or stratified cells with atypical hyperchromatic nuclei and prominent cytoplasm was observed, infiltrating all layers of the wall, serosa, and adjacent adipose tissue. Lymphatic invasion was also identified, although lymph node architecture remained preserved with sinus histiocytosis unaccompanied by tumor invasion. The diagnosis rendered was that of an ulcerated, well-differentiated, papillary adenocarcinoma grade II, invading all layers of the wall and adjacent adipose tissue (2.5 cm). Encouragingly, the surgical resection line and lymph nodes exhibited no evidence of tumor. Simultaneously, the adherent hepatic tissue depicted severe microsteatosis alongside portal inflammation and fibrosis. These findings were complemented by the hepatic biopsy measuring 0.5 cm, which indicated benign attributes inclusive of severe steatosis and chronic portitis. Based on the above findings and considering all previous radiological and interventional procedures, the Yokoyama/Kim/Nakata classification system for biliary tract tumors was used to aid in the development of a treatment plan for the patient's surgical procedure.

5. Discussion

Cystic duct adenocarcinoma, a rare medical condition, is classified as a variant of gallbladder cancer. The initial diagnostic parameters for identifying cystic duct adenocarcinoma were elucidated by Farrar et al. [3]. These parameters include: (A) localized growth confined to the cystic duct, (B) the absence of neoplastic processes within the gallbladder or biliary duct, and (C) the presence of histological evidence indicating the existence of adenocarcinoma. However, it should be noted that these criteria may not be entirely suitable for diagnosing cases in advanced stages where the neoplastic growth infiltrates adjacent anatomical structures. Subsequently, Ozden et al. [5] undertook a revision of these criteria, characterizing cystic duct adenocarcinoma as a specific type of gallbladder tumor primarily centered within the cystic duct. In either diagnostic approach, it is imperative that residual cystic duct carcinoma is discerned occurring at least 5 years post-cholecystectomy for precise definition [8]. In our specific case, the tumor exhibited characteristics in line with Type 1 in Kim's classification, CC type in Yokohama's classification, and Type I in Nakata's classification [9].

Consistent with the central focus of our research, the primary occurrence of cystic duct carcinoma has exhibited a notable prevalence among males, devoid of any observable gender predisposition. The typical age of onset, which coincides with previously documented findings at approximately 65 years (spanning from 38 to 79 years), corroborates earlier research [5]. While gallstones are not consistently implicated, they were identified in approximately a quarter of reported cases [10]. Notably, our specific case presented with the presence of pancreatic stones concomitant with inflammation. Despite the global delineation of diverse staging systems for various malignancies, it is pertinent to emphasize that, as of the current state of knowledge, no universally accepted diagnostic or staging framework has been universally established for cystic duct carcinoma, thus precluding the provision of a standardized and universally applicable approach [10].

The predominant clinical presentation consisted of abdominal

discomfort and jaundice, with both symptoms being equally prevalent. As reported by Baraka et al., in a study encompassing 33 documented cases, 81 % of individuals displayed right upper quadrant abdominal discomfort, 41 % manifested an abdominal mass, and four cases presented with obstructive jaundice [11]. Remarkably, in a significant majority of cases, ranging from 86 % to 93 %, gallbladder hydrops was observed. Typically, the detection of the tumor occurs either intraoperatively during laparotomy or subsequent to histopathological examination of the specimen [5]. It is noteworthy that none of the cases reported in the literature were diagnosed preoperatively. Likewise, in our specific case, the patient had a documented history of jaundice accompanied by upper abdominal pain, along with the presence of gallbladder hydrops, culminating in the definitive diagnosis being established through meticulous histopathological examination. In a majority of the cases reported, the diagnosis was made either prior to surgical intervention based on suspected clinical indications or postoperatively through histopathological analysis, mirroring the diagnostic course observed in our case [12].

Diagnostic imaging procedures, such as CT scans, ERCP, EUS, and POCS, assume a central role in the assessment and delineation of the extent of the disease. In the case under discussion, the patient's initial presentation, marked by general inflammation and clinical manifestations, notably right upper quadrant pain and jaundice, prompted their admission to the emergency department. Subsequently, this admission precipitated a comprehensive investigation that encompassed both radiological and histological analyses. This investigative approach enabled the timely and precise establishment of a diagnosis, thereby affording the patient the opportunity for decisive curative surgical intervention.

It is noteworthy that while the resectability rate for cancers of the extrahepatic bile duct or gallbladder is typically less than 30 %, in the majority of cases of cystic duct carcinoma (CDC), this rate approaches nearly 100 %. A contributing factor to this favorable outcome is the relatively lower incidence of lymph node metastasis in CDC patients, ranging from 0 % to 40 %, in contrast to those with extrahepatic bile duct cancer (approximately 50 %) or gall bladder cancer (40 % to 80 %) [13]. In the specific case we present, the patient's gall bladder exhibited a thickened wall, measuring up to 2 cm, and contained a 2.5 cm fungating mass within the cystic duct region. This mass exhibited a firm, white appearance upon sectioning. As a result, we performed the isolation of the entire length of the common bile duct and the cystic duct. The mass was located at the distal end of the cystic duct, proximate to its confluence with the common bile duct. Subsequently, we conducted a cholecystectomy in conjunction with the cystic duct, ensuring an adequate safety margin of approximately 1.5 cm. This procedure encompassed the removal of the cystic duct opening at the common duct, followed by the closure of the common duct stump. The endorsed therapeutic protocol entails a comprehensive surgical intervention, combining cholecystectomy with non-anatomical resection of the gallbladder fossa and the removal of the extrahepatic bile duct, coupled with regional lymphadenectomy, as elaborated in references [6]. Tumor dimensions typically average between 25 and 27 mm, with a range extending from 4 to 60 mm [5]. In our specific case, we adhere to a consistent approach, implementing the Roux-en-Y anastomosis technique. This technique involves establishing a biliary-jejunostomy to connect the remaining portion of the common duct with a jejunal loop, in addition to performing a jejunostomy procedure.

Diagnosing primary cystic duct carcinoma, which is challenging due to its similarity to other conditions, requires imaging tests (ultrasound, CT, MRI, or ERCP) and biopsy or cytology, following NCCN guidelines. In our case, ultrasound and CT scans led to the diagnosis post-surgical resection; however, molecular testing was unavailable, which could have identified therapy targets. Treatment complexity arises from factors such as tumor respectability, stage, patient status, and comorbidities. Surgical resection, the main curative treatment as NCCN guidelines, was performed in our case with Roux-en-Y anastomosis, indicating a complete resection. However, no neoadjuvant or adjuvant therapy was administered due to the patient's poor status and comorbidities. Such therapy, including chemotherapy, radiation, immunotherapy, or targeted therapy, could have mitigated recurrence risk. Managing cystic duct carcinoma can be a challenging task as it requires a multidisciplinary approach and close monitoring of the patient. According to the NCCN guidelines, the involvement of various specialists, such as surgeons, oncologists, radiologists, pathologists, gastroenterologists, and palliative care providers, is crucial for the care of patients with biliary tract cancers. However, in our case supportive care was provided, but faced certain limitations in our setting, such as the unavailability of molecular testing, targeted therapy, immunotherapy, and liver transplantation. Additionally, there was a scarcity of clinical trials and biomarker research for biliary tract cancers. These limitations could have affected the patient's prognosis and survival, highlighting the need for more resources and collaborations to improve the care of patients with biliary tract cancers in low- and middle-income countries [14]. Following surgical intervention, postoperative adjuvant radiation therapy emerges as a viable consideration for patients diagnosed with advanced cystic duct carcinoma, particularly those presenting positive surgical margins, as corroborated by authoritative sources. It is worth highlighting that reported data indicate a noteworthy contrast in average survival duration for such cases, averaging 27.2 months, which stands in stark contrast to the mere 5.8 months typically observed for gallbladder carcinoma and the range of 3.2 to 11.4 months noted in other cases involving the extrahepatic biliary ducts [15]. In a research study conducted by Nakata et al., a remarkable 5-year survival rate of 40 % was documented, accompanied by a median survival period of 2.4 years. This survival advantage was notably conspicuous among patients classified as Type I in comparison to their Type IV counterparts ($p = 0.05$). Conversely, no statistically significant disparities in survival rates were observed among patients harboring cystic duct carcinoma categorized as Types II, III, and IV [6]. Median overall survivals were established at 11.9 months for HH type and 45.8 months for CC type cases [15]. While advancements in imaging techniques and an enhanced understanding of the molecular underpinnings of this disease have contributed to a more profound comprehension of cystic duct carcinoma, it is discernible that a more comprehensive assessment involving a larger cohort of cases holds the potential to yield further profound insights. In our particular case, we conducted follow-up assessments at three and six months post-surgery. During these assessments, we observed a marked and substantial improvement in the overall condition of the patient.

6. Conclusion

This case report highlights the intricate nature of primary cystic duct carcinoma, an uncommon and aggressive biliary malignancy. A comprehensive analysis of clinical presentation, diagnostic challenges, and surgical management emphasizes the importance of multidisciplinary approaches in addressing complex neoplasms. The timely diagnosis and strategic interventions demonstrated in this case illustrate the importance of these approaches in optimizing patient outcomes. Further research and collaboration are crucial for advancing our understanding of this enigmatic entity and refining treatment strategies.

Consent

Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Ethical approval

Ethical approval for the study was obtained from the Ethical Committee of Damascus University, Faculty of Medicine, Syria.

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CRediT authorship contribution statement

JA, MJ, RH have participated in writing the manuscript. JA, MJ, RH reviewed the literature. All Authors critically and linguistically revised the manuscript. JA, MJ, RH, AA, MFA contributed to revision of the manuscript. JA prepared and revised the final manuscript. HH supervised the conduct of the study and performed the surgery. All authors read and approved the final manuscript.

Guarantor

Prof. Hamoud Hamed.

Research registration number

Not applicable (Because there are no NEW surgical techniques or technologies introduced).

Declaration of competing interest

The authors declare that they have no competing interests.

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