

CASE REPORT

An extremely rare case of distal common bile duct adenocarcinoma in a 65-year-old male patient

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Abstract

Cholangiocarcinoma is an extremely rare and highly aggressive primary malignancy of the biliary tract. The current report illustrates a rare case of distal common bile duct adenocarcinoma encountered in a 65-year-old male patient who was thoroughly investigated after presenting with a two weeks history of pain in the right hypochondrium, jaundice and unintentional weight loss (6 kg in two weeks). The medical team opted for a pancreaticoduodenectomy (Whipple procedure) managing to obtain negative resection margins of the tumor with a favorable immediate postoperative evolution. However, the surgical team was forced to reintervene twice due to complications caused mainly by the patient's disregard.

Keywords: cholangiocarcinoma, adenocarcinoma, computed tomography, pancreaticoduodenectomy.

Introduction

Biliary tract cancer is an extremely rare and highly aggressive malignant tumor considered to be the second most common primary malignancy located in the hepatobiliary structures with recent studies suggesting a continuous increasing incidence. According to the affected anatomic region, malignant tumors that develop in the biliary tract can be divided into gallbladder cancer, cholangiocarcinoma and ampullary cancer [1–3]. Furthermore, cholangiocarcinoma can be separated into three different entities: intrahepatic, perihilar and distal, with the latter two previously described as extrahepatic cholangiocarcinomas [4, 5].

Cholangiocarcinogenesis affects the perihilar area in around 50% of all cases. Some less common affected regions include intrahepatic cholangiocarcinoma (15%), middle (17%) and distal third of the common bile duct (18%) [6]. Malignant tumors of the distal common bile duct (CBD), ampullary and pancreatic head cancers are usually referred to as periampullary carcinomas due to multiple clinical similarities and silent evolution with unspecific signs and symptoms that are frequently ignored by the patient [7].

Aim

The current case report presents a male patient diagnosed with a rare form of adenocarcinoma located in the distal CBD and reveals details regarding the patient's clinical history, signs, symptoms, blood tests, imaging and histopathology findings and surgical treatment.

Case presentation

A 65-year-old male patient living in the urban area presented to the Emergency Department with a two weeks history of pain in the right hypochondrium, jaundice and unintentional weight loss (6 kg in two weeks). The patient is a former smoker who claims he quit smoking seven years ago. Also, he has worked for five years in a toxic environment (steel factory). Some of the previously known medical conditions of the patient include ischemic cardiomyopathy, essential arterial hypertension, benign prostatic hyperplasia and mixed hyperlipidemia. There was no link between malignant tumors and the patient's family history.

During the clinical examination, the patient presented jaundice and accused pain in the right hypochondrium. The initial liver blood tests revealed some major abnormalities (Table 1).

Table 1 – The initial liver blood tests accompanied by their recorded and normal values

Liver blood test	Recorded value	Normal values
Total bilirubin	11.52 mg/dL	0.2–1.3 mg/dL
Direct bilirubin	9.77 mg/dL	0–0.4 mg/dL
γ-Glutamyl transferase (GGT)	831 U/L	15–73 U/L
Aspartate aminotransferase (AST)	94 U/L	14–35 U/L
Alanine aminotransferase (ALT)	98 U/L	10–45 U/L

The patient's age, signs and symptoms indicated either a periampullary carcinoma or possible gallstones within the CBD. The first step of the diagnostic process was to

perform an abdominal ultrasonography (US). The US examination revealed multiple gallstones within the gallbladder and a normal sized liver with dilatation of the intrahepatic and extrahepatic bile ducts. The CBD measured 16 mm in diameter. A 10 mm hyperechoic area was described in the distal choledoch. Due to an inconclusive US report indicating significant changes affecting the biliary tract, the medical team maintained a high degree of clinical suspicion regarding a malignant tumor. Therefore, the next step of the diagnostic process was to further investigate the patient through computed tomography (CT).

The patient underwent an abdominal and pelvic CT examination after intravenous administration of a contrast agent. The CT investigation was performed on a Siemens Somatom Volume Zoom CT machine, which is an entry-level 4-slice CT scanner with a maximum table load of 200 kg/450 lbs, a maximum gantry aperture of 70 cm and a slice thickness ranging from 0.5 to 10 mm. The CT report indicated a normal sized liver with a significant dilatation of the intrahepatic bile ducts: the left hepatic duct measured 11 mm in diameter and the right hepatic duct measured 12 mm in diameter. The gallbladder had multiple gallstones inside with the largest one measuring up to 11 mm. The CBD measured 16 mm in diameter with no visible gallstones at this level (Figure 1). However, a

stenotic infiltrative process measuring 28 mm in length was described in the distal CBD (Figures 2 and 3). The pancreas had a normal aspect with no significant changes. This time, the CT report turned out to be extremely helpful and confirmed the medical team's initial suspicion.

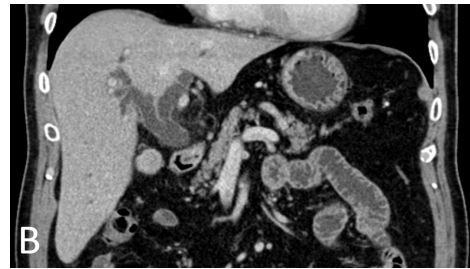
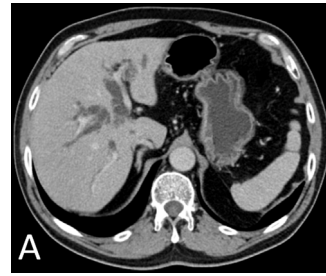


Figure 1 – The CT examination reveals a significant dilatation of the intrahepatic and extrahepatic bile ducts both on axial (A) and coronal (B) images.



Figure 2 – CT coronal images (A–C) show the stenotic infiltrative process (red arrow) located in the distal common bile duct with superjacent dilatation of the biliary tract.

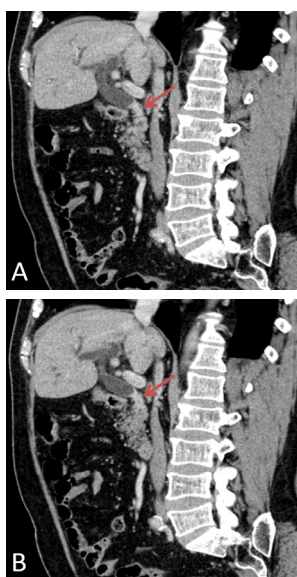


Figure 3 – CT sagittal images (A and B) show the stenotic infiltrative process (red arrow) located in the distal common bile duct with superjacent dilatation of the biliary tract.

Several days later, the patient underwent an endoscopic retrograde cholangiopancreatography (ERCP) examination, which confirmed the CT imaging findings and also revealed erosive areas accompanied by edema in the duodenal mucosa, with a normal aspect of the duodenal papilla. A dilatation of the affected distal common bile duct was performed, followed by the implementation of a double pigtail biliary stent (Figure 4, A–C). Several days after, the blood tests revealed a total bilirubin value of 5 mg/dL, while the recorded value for the direct bilirubin was 4.15 mg/dL. Also, the serum cancer antigen (CA) 19-9 was 245 U/mL with reference values being less than 37 U/mL.

Multiple investigations pointed towards a malignant tumor within the distal biliary tract. Therefore, the patient was scheduled for a pancreaticoduodenectomy (Whipple procedure) six days after the ERCP examination because of the required preoperative preparation. The immediate postoperative evolution of the patient was favorable as the medical team also opted for enteral and parenteral nutrition, multiple peritoneal drainage, complex treatment with antibiotics and pancreatic enzyme inhibitors. After the surgery was performed, the structures that were removed were sent in for histopathology evaluation.

The Hematoxylin–Eosin (HE) slides were scanned using a motorized Nikon 90–I microscope driven by the Nikon NIS Elements AR software package (Elta 90, Bucharest, Romania) in the Research Center for Microscopic Morphology and Immunology, University of Medicine and Pharmacy of Craiova, Romania. The histopathology report indicated a moderate to poorly differentiated bile duct adenocarcinoma infiltrating the choledoch. The lesion was infiltrating the muscularis propria and the surrounding stroma. Also, a massive perineural invasion was present.

The resection margins of the tumor were negative. The tumor staging after histopathology evaluation was pT2N0 (Figure 5).

The tumor cells were positive for cytokeratin (CK) 7 and negative for CK20. Based on anti- α -smooth muscle actin (anti- α -SMA) immunohistochemistry, the tumor was distorting and dissecting the smooth muscle laminae of the duct. The tumor had a variable Ki-67 mitotic index ranging between 20–70% of the tumor epithelium (Figure 6).

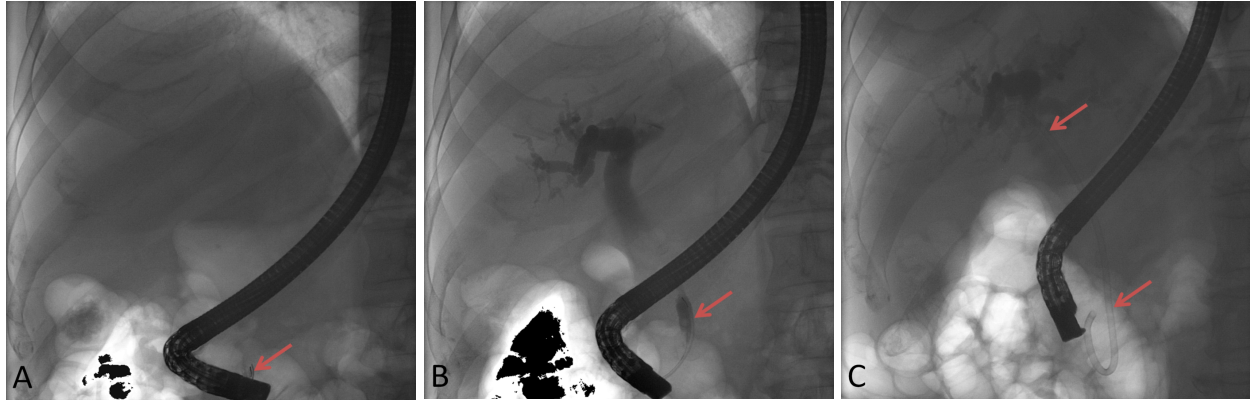


Figure 4 – The ERCP examination revealed erosive areas accompanied by edema in the duodenal mucosa, with a normal aspect of the duodenal papilla. After examining the duodenum, a plastic tube was inserted into the distal bile duct (A). A dilatation of the affected distal choledoch was performed (B), followed by the implementation of a double pigtail biliary stent (C).

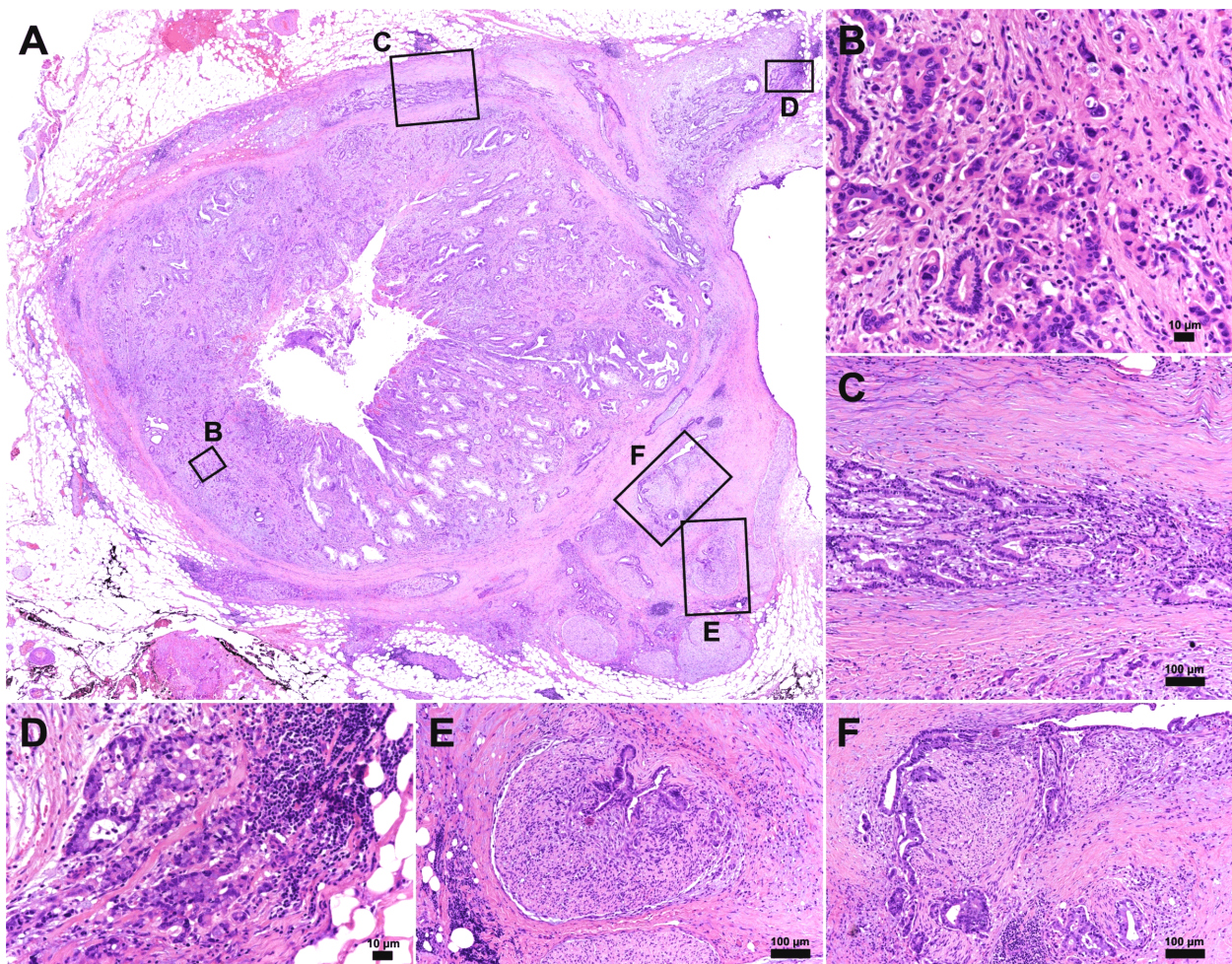


Figure 5 – Bile duct carcinoma infiltrating the choledoch (HE staining). Overview of the choledoch (A), infiltrated by a moderate to poorly differentiated tumor (B) that infiltrates the muscularis propria (C) and beyond in the surrounding stroma (D), with massive perineural invasion (E and F). Insets in (A) represent corresponding enlarged areas in images B–F.

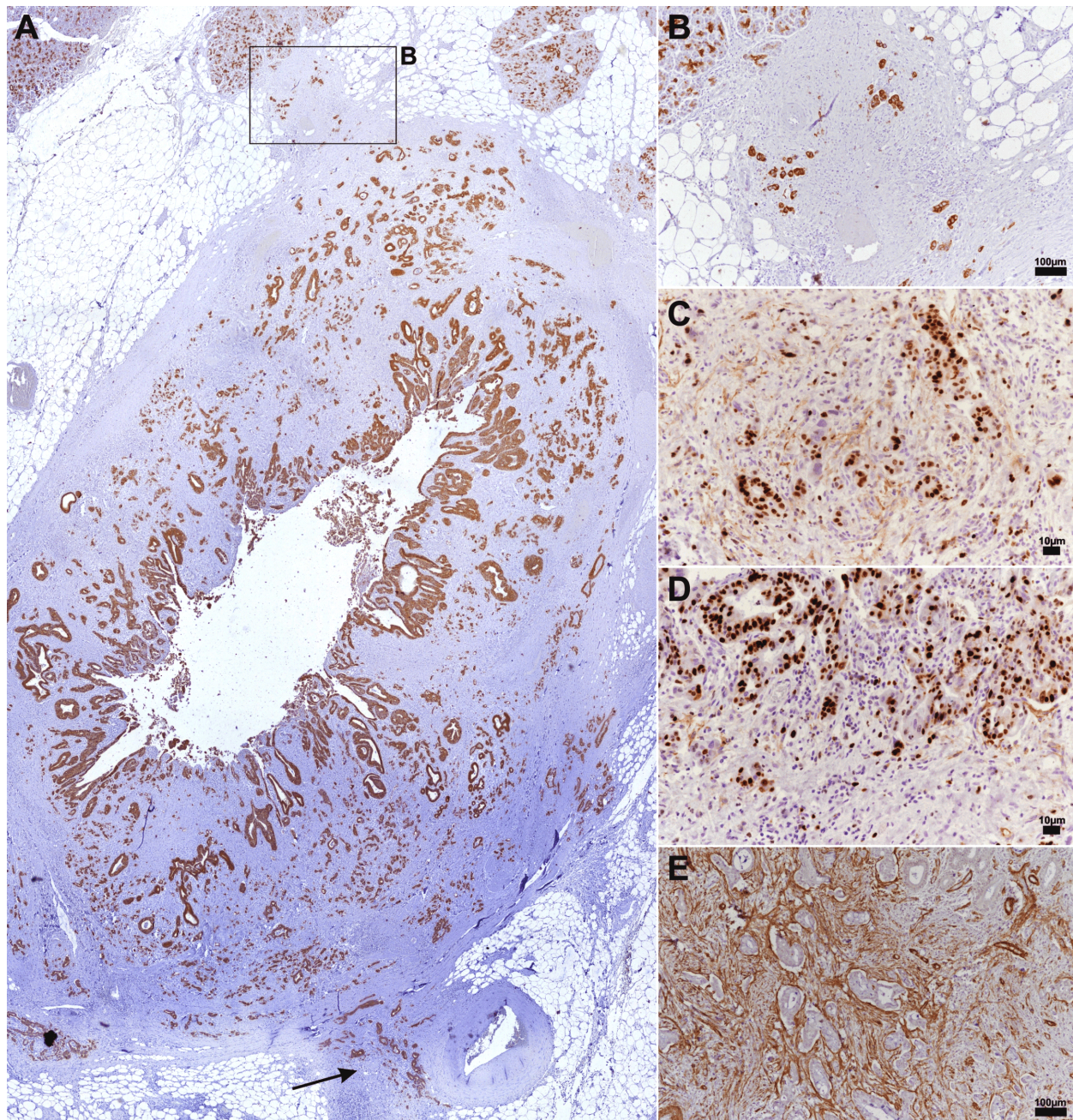


Figure 6 – Invasion throughout the wall of the duct visualized with an anti-CK7 antibody (A) with arrow around a peri-adventitial vessel; tumor glands extend to the close proximity of the pancreas (B), with a variable Ki-67 proliferation index around the tumor areas (C and D). The tumor is disorganizing the smooth muscle layer of the duct, as seen with an anti- α -SMA staining (E).

Eleven days after the surgery, the patient refused enteral and parenteral nutrition and ingested food, neglecting the doctors' multiple warnings. Not long after, the unfavorable evolution of the patient indicated either a possible fistula of the gastrojejunal anastomosis or an acute pancreatitis of the remaining pancreatic tissue. Both concerns of the medical team were confirmed in the 15th day after initial surgery when the subhepatic drainage revealed gastric content thus forcing the medical team to perform a new surgery. Acute necrotizing pancreatitis of the remaining pancreatic tissue and a minimal fistula affecting the gastrojejunal anastomosis were noticed upon initial inspection. The medical personnel opted for a restoration of the gastrojejunal anastomosis coupled with peripancreatic and peritoneal drainage. Despite the efforts

of the medical team, the patient started becoming increasingly uncooperative, manifesting behavioral and language disorders. The postoperative evolution of the patient remained critical.

Nine days after reintervention, the drainage tubes revealed gastric fluid once again. This time, the gastric content came from a gastric perforation measuring 1 cm, located away from the gastrojejunal anastomosis. Also, the acute necrotizing pancreatitis complicated with multiple intermesenteric abscesses. The surgical team sealed the gastric perforation and reinforced it by using the epiploon. Also, doctors continued the multiple peritoneal drainage and considered that a Witzel feeding-jejunostomy was more suitable for the patient. The dynamic evolution of the patient's blood tests is illustrated in Table 2.

Table 2 – The dynamic evolution of the patient's blood tests. The ERCP procedure was performed in the 7th day. The initial surgery that involved pancreaticoduodenectomy using Whipple's procedure took place in the 13th day. The restoration of the gastrojejunal anastomosis was completed during the first reintervention in the 24th day, while the second and final reintervention took place in the 37th day

Day	Blood test results				
	Total bilirubin [mg/dL]	WBC count [$\times 10^3/\text{mcL}$]	Hb [g/dL]	Ht [%]	Blood sodium [mmol/L]
1	11.52	8.56	15.7	46.5	143.38
12	5	7.68	13	39.8	143.73
14	4.2	13	11.3	34.7	144.05
23	1.67	14.1	11.1	35.1	166.8
28	1.16	9.7	8.9	27.1	158.3
36	0.67	7.2	9.4	29.5	158.14
38	0.69	8.6	9.5	29.4	156.71

ERCP: Endoscopic retrograde cholangiopancreatography; WBC: White blood cell; Hb: Hemoglobin; Ht: Hematocrit.

Discussions

The incidence values of cholangiocarcinomas throughout the world range from 1–2 per 100 000 in regions such as Europe and the USA to 2–4 per 100 000 in Southeast Asia [8]. The Asian population is usually affected by up to two times more frequently than the rest of the world mainly due to the liver fluke infestations. Cholangiocarcinoma commonly targets men in their 6th–7th decade [9, 10]. Some acknowledged risk factors for developing biliary tract cancer include liver fluke infestations, primary sclerosing cholangitis, hepatolithiasis and choledochal cysts. More recent studies suggest a potential link between cholangiocarcinogenesis and hepatitis B virus, hepatitis C virus, liver cirrhosis, diabetes and human immunodeficiency virus [11–13]. However, it is not uncommon for patients to develop cholangiocarcinoma in the absence of any identifiable risk factors [14].

The histopathological results indicate the tumor is an adenocarcinoma in over 95% of all cases with a histological grade ranging from undifferentiated to well differentiated [15]. Adenocarcinomas are commonly associated with esophageal, breast, pancreas, prostate and colon cancers due to the high frequency of glandular structures at these levels. Furthermore, pulmonary adenocarcinomas account for nearly 40% of all lung tumors and usually affect younger non-smoker females [16]. Some of the less common tumor types include adenosquamous carcinoma, small cell carcinoma and squamous cell carcinoma.

Regarding the clinical aspects, malignant tumors of the distal choledoch are difficult to diagnose before they reach advanced stages due to a silent evolution with unspecific signs and symptoms that are usually ignored by the patient. However, as the disease progresses, the patient notices an abnormal skin color (jaundice) and a significant weight loss in a short period of time without any dietary changes. Other signs and symptoms include fatigue, weakness and night sweats [1].

Distal CBD malignant tumors can be assessed with the help of imaging methods like US, CT, ERCP and

magnetic resonance cholangiopancreatography (MRCP). US is generally used for the initial evaluation of the patient, being able to detect possible lesions of the liver and stones or dilatations along the biliary tract. Any suspicious changes noticed initially on US images indicate that further imaging methods are required, especially for differentiating from other primary liver malignancies such as hepatocellular carcinoma [16–18]. For example, imaging methods like CT or MRCP can detect more accurate changes like bile duct wall thickening or evaluate the biliary, parenchymal, lymphatic and vascular extension of a tumoral mass. ERCP is both a diagnostic and therapeutic invasive procedure considered to be extremely valuable due to the possibility to provide tissue samples through various techniques and also to place biliary stents [19, 20].

Treatment options are rather limited, with surgery remaining the main procedure. While some non-invasive techniques, such as photodynamic therapy and radio-frequency ablation have been studied after being adopted in hepatic tumors, distal CBD malignancies still require a pancreaticoduodenectomy (Whipple procedure) [21, 22]. This type of surgery usually requires around 5–8 hours to complete and involves the removal of the gallbladder, the CBD, the pancreatic head and the surrounding lymph nodes, the duodenum and the distal part of the stomach (antrum). The remaining structures (the body and tail of the pancreas, the stomach and the bile duct) are then reattached to the remaining jejunum in order to reestablish the normal circulation and digestion of the food. The lymph nodes are often found positive compared to the intrahepatic and perihilar forms of cholangiocarcinoma. The most vital predictor regarding the patient's survival is represented by the negative margins of the tumor. If this condition cannot be accomplished through surgery then the patient will undergo chemotherapy [4, 23, 24].

Conclusions

The current report illustrates a rare case of a distal common bile duct adenocarcinoma encountered in a 65-year-old male patient who was thoroughly investigated. The medical team opted for a pancreaticoduodenectomy (Whipple procedure) managing to obtain negative resection margins of the tumor with a favorable immediate post-operative evolution. However, the patient ignored the guidance of the medical personnel, forcing them to reintervene twice due to complications.

Conflict of interests

The authors declare that they have no conflict of interests.

Author contribution

Lucian Mihai Florescu and Ioana Andreea Gheonea equally contributed to the manuscript.

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