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A case report of intraoperatively diagnosed holangiocarcinoma after unsuccessful conservative treatment of ERCP complicated with hemorrhage

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Background

Cholangiocarcinoma is a malignant tumor arising from the epithelium of the bile ducts. Most of these tumors are adenocarcinomas [1]. Intrahepatic cholangiocarcinoma accounts for 10% of all cholangiocarcinomas, hilar cholangiocarcinoma for 25%, and extrahepatic cholangiocarcinoma for 65% [2, 3]. Cholangiocarcinoma can develop in any part of the extrahepatic duct, occurring in 50–75% of reported cases in the upper third of the duct including the hepatic hilum, in 10–25% in the middle third, and in 10–20% in the lower third [4–6]. Approximately 95% of cases show extrahepatic obstruction at the time of diagnosis [7]. In a meta-analysis of 21 prospective trials, the rate of hemorrhage as a complication of ERCP was 1.3% (95% CI, 1.2%–1.5%) with 70% of the bleeding episodes classified as mild [8]. Hemorrhagic complications may be immediate or delayed, with recognition of occurring up to 2 weeks after the procedure. The risk of severe hemorrhage (ie, requiring >5 units of blood, surgery or angiography) is estimated to occur in fewer than1 per 1 000 sphincterotomies [9]. Despite new and advanced diagnostic methods, sometimes this type of tumor is finally diagnosed from pathological findings on excised tissue.

Case report

We present one case with cholangiocarcinoma diagnosed after surgical treatment of hemorrhage as post procedural complication from ERCP. With MRCP intraluminal stenosis of the upper part of common bile duct has been noticed and suspicious presence of substrate with consecutive dilatation of the upper billiary tract. ERCP was performed and sphincterotomy have been made without evacuation of any intraluminal substrate from common bile duct. Insufficient ERCP cholangiography was made and biopsy of the part with stenosis could not be taken due to permanent bleeding from performed sphincterotomy. Despite all attempts for conservative treatment of the hemorrhage, patient was still with permanent decreases of hemoglobin levels and with persistent hemorrhagic anemia. With decision from medical council the patient has been transferred to the Department of abdominal surgery for further immediate surgical treatment.

Conclusion

Patient with extrahepatic bile duct carcinoma initially diagnosed as a calculus in the common bile duct. Looking back, the patient had symptoms which differential diagnosis for bile duct cholangiocarcinoma should be established. Clinical symptoms such as right hypochondrium pain, itchy skin, vomiting and diarrhea. The laboratory findings showed constantly elevated bilirubin and liver enzymes also elevated tumor markers as CA19-9 and CEA.

Hemorrhage that occurs after ERCP sphincterotomy and attempt for biopsy could not been controlled with conservative measures.

Patient with consequently caused hemorrhagic anemia has been transferred for surgical treatment, which stopped the bleeding, made final diagnosis and treatment of proximal stenosis of common bile duct.

Key words: cholangiocarcinoma, ERCP hemorrhage, billiary stenosis.

Introduction

Most patients with bile duct cancer are diagnosed in an advanced stage [10–12].

To improve the therapeutic effect of bile duct carcinoma, efforts have been focused on diverse areas: early detection of the lesions, accurate differentiation of benign and malignant biliary stenosis, and assessment of loco regional tumor extension, development of surgical methods, biliary stenting, and chemo radiotherapy for unresectable bile duct cancer [13].

In the diagnosis of intrahepatic cholangiocarcinoma, non-invasive, cross-sectional imaging tests including computed tomography (CT) and magnetic resonance imaging (MRI) are useful [13].

MRI in the form of magnetic resonance cholangiopancreatography (MRCP) and multi-detector low CT (MDCT) are the most commonly performed imaging tests in these patients. In contrast, for the diagnosis of extrahepatic bile duct cancer, an endoscopic approach is essential, for the simple reason that endoscopic techniques are more invasive and include the use of endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasonography (EUS) [13]. In the middle and distal bile duct, ultrasonography (US) cannot assess tumors sufficiently due to disturbance by gastrointestinal gas [14].

Even now, the sensitivities of US in demonstrating hilar tumor, middle bile duct tumor, and distal bile duct tumor are 85.6%, 59.1%, and 33.3%, respectively [14]. Therefore, bile duct dilatation on US findings is an important sign for the early diagnosis of bile duct cancer [14]. Until recently, when US showed dilatation of the bile duct, ERCP was the next step to obtain cholangiography. Recently, MRCP has become an alternative to ERCP as it is a non-invasive modality [15, 16]. When US shows intraductal tumor, initial ERCP rather than MRCP should be carried out for cost-effectiveness, even if the patient shows no jaundice. However, when US show only dilatation of the extrahepatic bile duct, MRCP is a safe modality to obtain a clear cholangiogram. On ERCP or MRCP findings, benign diseases including post-operative stenosis, chronic pancreatitis, primary sclerosing cholangitis, or autoimmune pancreatitis show bile duct stenosis as well as malignant disease [17–19]. Cholangiography shows filling defects at the common bile duct in patients with adenomyoma [17] or inflammatory strictures [18]. Therefore, accurate distinction between benign and malignant biliary structures is essential to avoid unnecessary surgery. The accuracy of MRCP is comparable with that of ERCP[19]. Malignancy is suggested when cholangiography shows long (greater than 10 mm), asymmetric, and irregular strictures. Benign disease is suggested when cholangiography shows short, regular, and symmetric strictures. Using these criteria, the diagnostic sensitivity and specificity for ERCP were 74% and 70%, respectively. The diagnostic sensitivity and specificity for MRCP were 70% and 72%, respectively [19].

Accurate diagnosis of the extent of the cancer is essential to enable selection of the appropriate medical and surgical therapy [13].

On dynamic CT findings, extrahepatic cholangiocarcinoma may be seen as a focal thickening of the ductal wall with various enhancement patterns. Until now, in many cases of extrahepatic cholangiocarcinoma, visualization of the tumor was not definitive because they were too small to be detected [12, 16, 20–31]. Extrahepatic bile duct carcinoma shows longitudinal spread

along the bile duct, often resulting in residual tumor at the surgical margin [13]. The length of longitudinal extension is determined by the type of invasion, with a mean length of 6–10 mm for the submucosal spread and 10–20 mm for the mucosal spread [34, 35]. MDCT correctly revealed longitudinal extension of extrahepatic cholangiocarcinoma in 62.5%–78.6% of patients [36, 37]. However, CT has a strong tendency to underestimate longitudinal mucosal spread, which is common in extrahepatic cholangiocarcinoma [38–46]. Tompkins et al [10] reported that 91% of patients with bile duct cancer who underwent surgery had serum bilirubin levels greater than 2.0 mg/dL. This is a case presentation about a female patient initially considered to have calculus, turned out to have cholangiocarcinoma in the common bile duct.

Case presentation

Female patient, aged 61, had diarrhea and was vomiting for two weeks. She had moderate to severe pain in the epigastrium and right hypochondrium.

She vomited only gastric contents several times, no blood or mucus was presented in her stool either. She also started to feel itchy, and her skin became more sensitive than usual. She consulted her general physician, who scheduled ultrasound of the abdomen and appointed laboratory tests.

Laboratory findings

Aspartat aminotransferase (AST) – 885 U/L, alanine aminotransferase (ALP) – 768 U/L, alkaline phosphatase (ALP) – 456 U/L, gamma glutamyl transferase (GGT) – 2 098 U/L, total bilirubin – 64 umol/L, direct bilirubin – 55 umol/L.

Ultrasound findings

Ultrasound of the abdomen showed that the gall bladder was with hyper echoic and thickened walls up to 4–5 mm, and the walls were in layers towards the fundus, without detectable calculus in the lumen. Furthermore, the ultrasound showed that common bile duct (ductus choledochus) was dilatated up to 12 mm in diameter, without ultrasound detectable intraluminal defect, while the intrahepatic biliary stem was emphasized and initially dilated.

Because of the fore mentioned ultrasound finding and laboratory results, the patient was hospitalized with a working diagnosis for calculus in the common bile duct, for additional investigations and treatment, at the Intensive care and emergency medicine department at the City General Hospital (8th of September) in Skopje.

Physical exam

Without deviations in the review of systems, with the exception of the pale yellow colored skin (her sclera was also yellow), and pain on palpation in right hypochondrium.

Other investigations

During her hospitalization, many laboratory tests and interventions were performed, as protocol requires. Her electrocardiogram (ECG) was unremarkable. Her total bilirubin, direct bilirubin, as well as the transaminases were all significantly elevated. Another ultrasound of the abdomen was performed.

The ultrasound showed an iso-echoic and homogeneous liver, with expected size and shape, with present intrahepatic dilatation of the biliary tract, without focal defects. The gall bladder had thickened walls, but without calculus in the lumen. The common bile duct (ductus choledochus) was dilated up to 16 mm, and had thickened walls as well. In the visible part calculus has not been noted.

However the pre-papillary region was unavailable for ultrasound assessment and therefore no final conclusion was made. The pancreas was non-homogeneous in the area of its head, while the rest of the gland was without alteration. Other findings on the abdominal organs were without clinical significances.

No free fluid was detected in the abdomen.

Additionally serum analysis for CA 19–9 and CEA tumor markers has been made.

CA 19–9 – 51,5 U/ml and CEA – 7,2 ng/ml.

These findings were still inconclusive, so the doctors decided to perform magnetic resonance imaging (MRI) of the abdomen with (MRCP) magnetic resonance cholangiopancreatography.

MRCP

The finding clearly presented an enlarged head of the pancreas, with no restriction to diffusion. In addition,

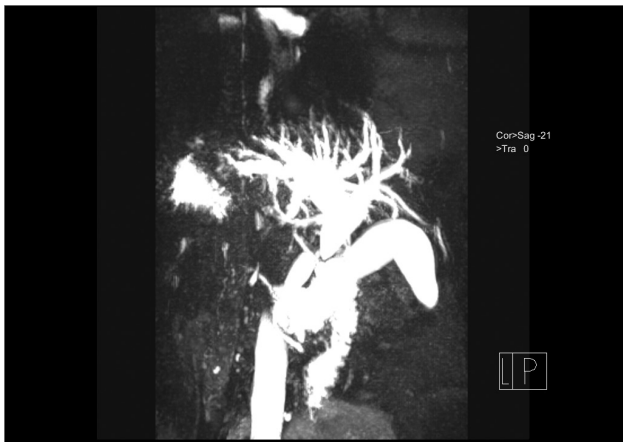

Figure 1.

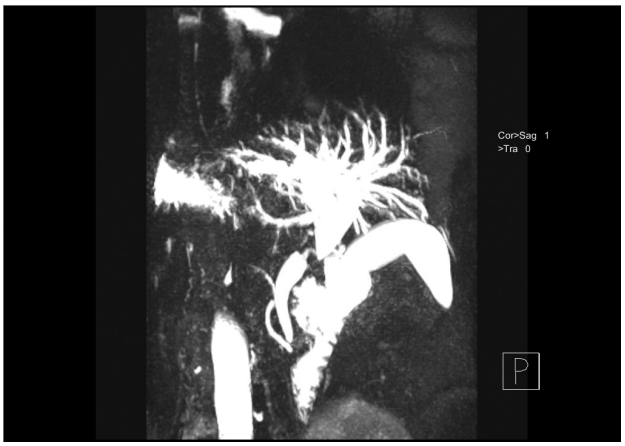

Figure 2.

there was a reduction of the lumen of the upper part of common bile duct and high presence of the substrate with consecutive dilatation of the common bile duct, and the hepatic duct to the right and to the left as well, with a maximum measured diameter of 15 mm. (Figure 1 and 2).

Further evaluation with endoscopic retrograde cholangiopancreatography (ERCP) was recommended.

ERCP

ERCP was performed and sphincterotomy have been made without evacuation of any intraluminal substrate from common bile duct.

Insufficient ERCP cholangiography was made and biopsy of the part with stenosis could not be taken due to permanent bleeding from performed sphincterotomy.

We do not have data for any intervention performed for treatment of bleeding during this procedure.

Because hemorrhage has been occurred during medical procedure, additional test has been performed.

Hematology findings

Hb – 75 g/L; Hct – 22.4%; RBC – $3.10x10^{12}$/L; WBC – $12.3x10^{9}$/L; PLT – $193x10^{9}$/L.

Coagulation tests

Prothrombin time (PT) – 16.1 second, activated partial thromboplastin time (aPTT) – 44 seconds, international normalized ratio (INR) – 1.3.

Patient without history of any anticoagulant and antiagregation medication intake

Laboratory tests

Aspartat aminotransferase (AST) – 435 U/L, alanine aminotransferase (ALP) – 368 U/L, alkaline phosphatase (ALP) – 246 U/L, gamma glutamyl transferase (GGT) – 798 U/L, total bilirubin – 55 umol/L, direct bilirubin – 43 umol/L.

Specialist in transfusion medicine was consulted and therapy with two units of FFP (fresh frozen plasma) was administered, also with 1 Erythrocyte concentrate unit (350 ml) and therapy with Vitamin K intravenously have been started.

Twelve days after hospital admission and one day after ERCP, patient was still slightly anemic with continuous decreasing of hemoglobin, erythrocyte count and hematocrit. Coagulation test were normalized.

Patient report two black stools, one day after ERCP was performed.

Administration of one erythrocyte concentrate unit (350 ml), FFP and therapy with colloids and crystalloid solution have been continued.

Medical consilium from gastroenterohepathologist, general surgeon and transfusiologist have been held second day after ERCP.

A decision was made and patient for further surgical treatment was transferred to the Department of abdominal surgery in CGH 8th September in order

to get surgical treatment for the bleeding from ductus choledochus, which caused the anemia in the first place. Another reason for transferring the patient to the surgical department however, was the fact that the imaging showed a suspicious stenosis at the proximal part of the common bile duct (ductus choledochus).

Surgical procedure

After all the pre-surgical preparations were made the patient was operated in general anesthesia. Intraoperative, by ligation and resection of the cystic artery and the cystic duct anterograde cholecystectomy was first performed.

The next step was mobilization of the common bile duct (ductus choledochus), after which in its proximal part a mass forming tumorous formation was observed. The tumor formation of the common bile duct (ductus choledochus) occupied 2/3 of the circumference of the wall, in total length of 1 cm. During the surgery, a decision was made to continue with supraduodenal resection of common bile duct, after prior ligation of the inbred vessels.

Intraluminally in common bile duct thrombotic masses were observed.

The fatty pillow from hepatoduodenal ligament and hepatic hilus has been removed without macroscopic enlarged lymph nodes.

The jejunal loop was mobilized and a terminal-lateral (T-L) anastomosis of the distal end was formed with the common hepatic duct with the jejunum, followed by an entero-entero anastomosis (EEA) according to Braun.

The postoperative course of the patient went smoothly, with established intestinal peristalsis and passage, as well as oral feeding.

The pathohistology finding was – Cholangiocarcinoma of the common bile duct in its proximal part (Latin: cholangoracinoma ducti choledochi partis proximalis). Tumor was in Stage I according to pTNM classification.

The patient, as per protocol, was referred to the University Clinic of radiotherapy and oncology, for adjuvant therapy.

Discussion

Preoperative evaluation of bile duct cancer in terms of radical resection consists of a multidisciplinary approach with ultrasonography (US), helical-computed tomography, magnetic resonance imaging (MRI) including MR cholangiopancreatography (MRCP), direct cholangiography *via* endoscopic retrograde cholangiography (ERC) or percutaneous transhepatic biliary drainage (PTBD), intra-ductal US (IDUS), and bile cytology or biopsy [47].

Several advances have been made in the surgical management of bile duct cancer within the last two decades. Surgical morbidity and mortality have been dramatically decreased, but the long-term outcome remains poor [48].

Complete surgical resection with a microscopically negative margin is the only factor under the control of the surgeon and is therefore the most important goal of surgical treatment [48].

A recent study emphasized the significance and accuracy of intraoperative assessment of bile duct margin [50], while a positive bile duct margin itself seems to have minimum impact on patient survival [51–53].

As noted above, there is a close association between the extent of the hepatic resection and the rate of negative margins in hilar cholangiocarcinoma [54]. These factors all warrant an aggressive surgical approach to bile duct cancer. Because of the high rate of recurrence and poor survival after radical surgery, postoperative chemotherapy, radiotherapy, and chemo-radiation have been evaluated in terms of improving patient survival after resection of bile duct cancer [49].

Conclusion

Patient with extrahepatic bile duct carcinoma initially diagnosed as a calculus in the common bile duct. Looking back, the patient had symptoms which differential diagnosis for bile duct cholangiocarcinoma should be established. Clinical symptoms such as right hypochondrium pain, itchy skin, vomiting and diarrhea. The laboratory findings showed constantly elevated bilirubin and liver enzymes also elevated tumor markers as CA19-9 and CEA.

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