

A Challenging Case of Recurrent Cholangitis Caused by Isolated Bile Duct Metastasis of Colorectal Adenocarcinoma: Rescue Therapy through Endoscopic Ultrasound-Guided Hepaticoesophagostomy

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Keywords

Biliary metastasis · Endoscopic ultrasound-guided hepaticoesophagostomy · Malignant biliary obstruction

Abstract

A 64-year-old male was admitted with fever, abdominal pain, and jaundice. Medical history was relevant for colorectal adenocarcinoma 11 years before and right hepatectomy due to liver metastasis. MRCP revealed left hepatic duct stenosis without liver nodules. ERCP was performed for biliary drainage with plastic stents. After inconclusive brush cytology, cholangioscopy (SpyGlass™ DS2) was performed showing villous mucosa surrounded by irregular vessels suggestive of tumor neovascularization. SpyBite™ biopsies confirmed biliary metastasis of colorectal origin. The patient started palliative chemotherapy being readmitted 6 months later with acute cholangitis. Diffuse infiltrating intrabiliary lesion with 120 mm was detected in control MRCP. Given its intraductal extension and gastric compression by the hypertrophied liver leading to duodenoscope mispositioning, transpapilar stents could not be deployed.

Multiorgan dysfunction developed despite broad-spectrum antibiotics, and EUS-guided biliary drainage was proposed. Although EUS access was limited by gastric bulging, puncture of a dilated intrahepatic duct was accomplished with a 19G needle. PCSEMS (GIOBOR™ 8 × 100 mm) placement was only possible above the gastroesophageal junction with the proximal flare being incidentally deployed in a 3-cm intraparietal esophageal tract. The misplaced stent was immediately recanalized, and a stent-in-stent FCSEMS (WallFlex™ 80 × 10 mm) allowed the hepaticoesophagostomy creation. Since the stent opening was orally oriented in esophageal lumen, parenteral nutrition was started to avoid contamination. Sepsis recovering and liver test normalization were observed. Before hospital discharge, stent reposition was planned to resume oral feeding. After placement of a third stent-in-stent NCSEMS (WallFlex™ 120 × 10 mm) in the hepaticoesophagostomy to prevent migration, the proximal flare was oriented to the stomach gently pushing with the endoscope aiding by an inflated biliary balloon. The patient resumed chemotherapy but died 8 months after due to disease progression. Isolated bile duct metastasis is an uncommon complication of

colorectal cancer. EUS-guided hepaticoesofagostomy is feasible when puncture through the esophagus was inevitable, especially in patients with liver hypertrophy.

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Colangite aguda recorrente por metástase biliar isolada de adenocarcinoma colorretal: terapêutica de resgate com hepaticoesofagostomia guiada por ecoendoscopia

Palavras Chave

Metástase biliar · Hepaticoesofagostomia guiada por ecoendoscopia · Obstrução biliar maligna

Resumo

Homem de 64 anos, admitido por febre, dor abdominal e icterícia. A história pregressa inclui adenocarcinoma colorretal há 11 anos e hepatectomia direita por metástases. A CPRM revelou estenose do ducto hepático esquerdo sem nódulos parenquimatosos evidentes. A CPRE foi realizada para drenagem biliar com próteses plásticas. Após citologia inconclusiva, foi efetuada colangioscopia (SpyGlass™ DS2) que revelou mucosa de aspeto viloso com vasos tortuosos e irregulares sugestivos de neovascularização tumoral. As biópsias foram compatíveis com metástase biliar de origem colorretal. O doente iniciou quimioterapia paliativa, tendo sido readmitido seis meses depois por colangite aguda. A CPRM revelou lesão intrabiliar infiltrativa difusa com 120 mm. Dada a sua extensão intraductal e o abaulamento gástrico condicionado pela hipertrofia do fígado remanescente, não foi possível a colocação de novas próteses por acesso transpapilar. O quadro clínico evoluiu desfavoravelmente com disfunção multiorgânica apesar da antibioterapia de largo espectro. Neste contexto foi proposta drenagem biliar guiada por ecoendoscopia. Com recurso a um ecoendoscópio linear, foi possível a punção de um ducto biliar intra-hepático dilatado com agulha de 19G. A libertação de prótese parcialmente coberta (GIOBOR™ 8 × 100 mm) foi apenas possível acima da junção esofagogastrica, resultando na libertação acidental da extremidade proximal num trajeto intraparietal esofágico. A prótese foi imediatamente recanalizada e colocada uma prótese totalmente coberta (WallFlex™ 80 × 10 mm) pela técnica stent-in-stent, permitindo a criação da hepaticoesofagostomia. Uma vez que a prótese se encontrava orientada para a cavidade oral, foi instituída nu-

trição parentérica total para evitar contaminação biliar. Verificou-se melhoria da sépsis e normalização das provas hepáticas durante o restante internamento. Previamente à alta foi agendado novo procedimento para retomar a via oral. Após a colocação de uma prótese biliar não coberta (WallFlex™ 120 × 10 mm) na hepaticoesofagostomia pelo método stent-in-stent, com auxílio de balão de extração de cálculos procedeu-se à mobilização da extremidade esofágica da prótese para o estômago. O doente retomou quimioterapia, tendo falecido oito meses depois por progressão da doença. As metástases biliares isoladas constituem uma complicação rara do cancro colorretal. A hepaticoesofagostomia guiada por ecoendoscopia é possível quando a punção do esófago é inevitável, nomeadamente em doentes com hipertrofia do lobo hepático esquerdo.

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Introduction

Colorectal cancer (CRC) is one of the most common digestive tract malignancies worldwide being the second leading cause of cancer death [1]. Owing to screening/early detection programs and effective therapeutic approaches, the life expectancy of CRC patients can be remarkably prolonged [2]. However, up to 20% of patients diagnosed with CRC have already metastatic disease, whereas another 25% will develop metastases later in life [3, 4]. The most common site for CRC metastasis is the liver, followed by the lungs, peritoneum, and distant lymph nodes [5]. Isolated bile duct metastasis is an extremely rare manifestation of CRC, and therefore, no evidence-based guidelines on the management of this entity are available [6, 7].

Endoscopic ultrasound-guided biliary drainage (EUS-BD) has been regarded as the procedure of choice in patients with malignant biliary obstruction after failed endoscopic retrograde cholangiopancreatography (ERCP) [8]. In reference centers, EUS-BD has higher clinical success, lower rate of adverse events, and fewer need for re-intervention compared with percutaneous transhepatic drainage [9]. Nevertheless, EUS-guided hepaticogastrostomy (HGS), commonly recommended for hilar obstruction, may not be always technically possible. EUS-guided hepaticoesofagostomy (EUS-HES) is emerging as a rescue procedure in patients with malignant biliary obstruction when puncture through the esophagus is inevitable [10]. The authors describe a

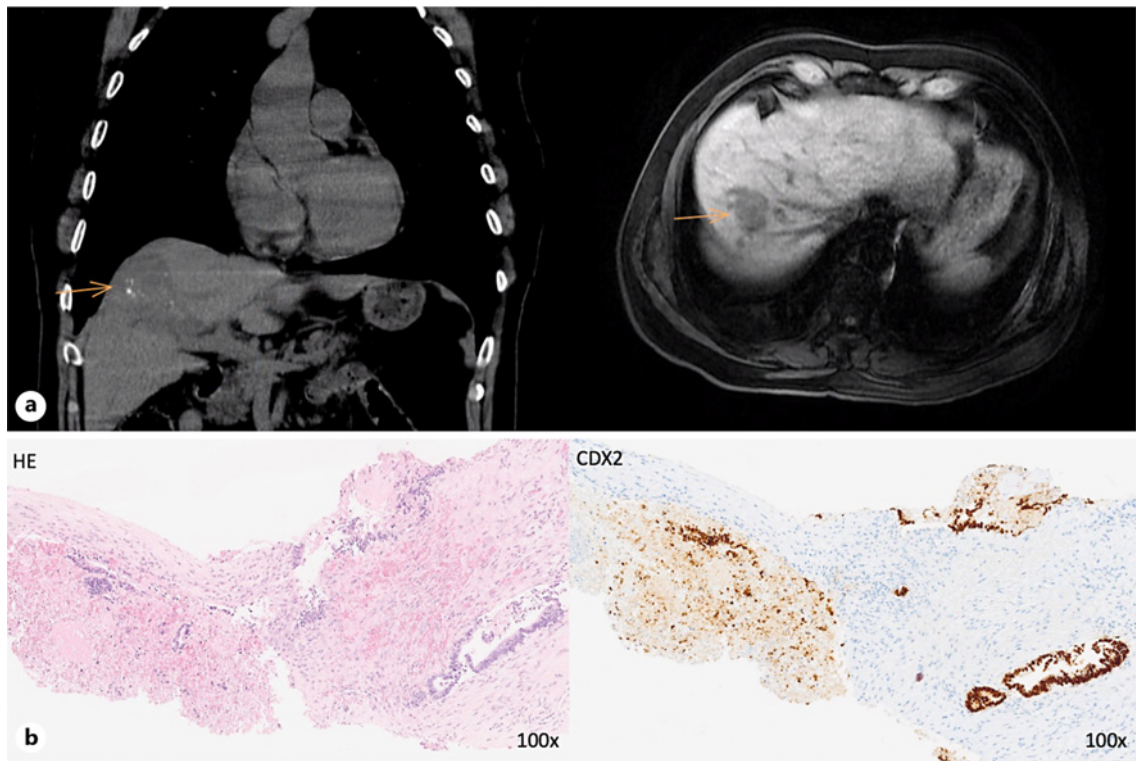


Fig. 1. a Two liver nodules with 1.8 cm and 3.7 cm detected on CT/MRI after 8 years of follow-up. **b** Surgical pathology confirmed metastases of colorectal adenocarcinoma after liver resection.

challenging case of recurrent cholangitis due to biliary metastasis of CRC which ended in a EUS-HES for biliary drainage.

Case Report

The authors present the case of a 64-year-old male admitted in the gastroenterology ward due to abdominal pain, jaundice, and fever. Past history was relevant for sigmoid adenocarcinoma (T3N2M0), being submitted to left hemicolectomy plus adjuvant chemotherapy (FOLFOX regimen) 11 years before. On follow-up (8 years after CRC diagnosis), two liver nodules with 1.8 cm and 3.7 cm located in segments 4 and 8 were detected on surveillance CT and further characterized on MRI (Fig. 1). The patient started chemotherapy (FOLFOX) and cetuximab and underwent right hepatectomy plus segmentectomy (4b) with disease remission during the last 3 years. Surgical pathology confirmed the metastases of colorectal adenocarcinoma.

In the gastroenterology ward, tumor markers were increased (CEA 35; CA 19.9 300) and a magnetic reso-

nance cholangiopancreatography showed left hepatic duct stenosis with no evidence of liver nodules. ERCP confirmed proximal common bile duct/left hepatic duct stenosis, and biliary drainage was accomplished with plastic stents (Fig. 2). Brush cytology was inconclusive but suspicious for malignancy.

After multidisciplinary discussion, it was decided to repeat ERCP with peroral cholangioscopy in order to perform target biopsies and lesion roadmap as the patient could be a potential candidate for liver transplant. Cholangioscopy (SpyGlass™ DS2) showed villous mucosa surrounded by irregular vessels suggestive of tumor neovascularization involving all the bile duct from the ampulla to the hilum. SpyBite™ biopsies were performed, and histology revealed biliary metastasis of adenocarcinoma. Immunohistochemistry was positive for CDX2/CK20/SMAD4 and negative for CK7, being suggestive of colorectal origin (Fig. 3). Due to hilum involvement in a patient with previous liver surgery (right hepatectomy plus segmentectomy), common bile duct resection and hepaticojejunostomy were not considered in this regard. PET-FDG was further requested for disease restaging and displayed new hypermetabolic foci in the lung compatible

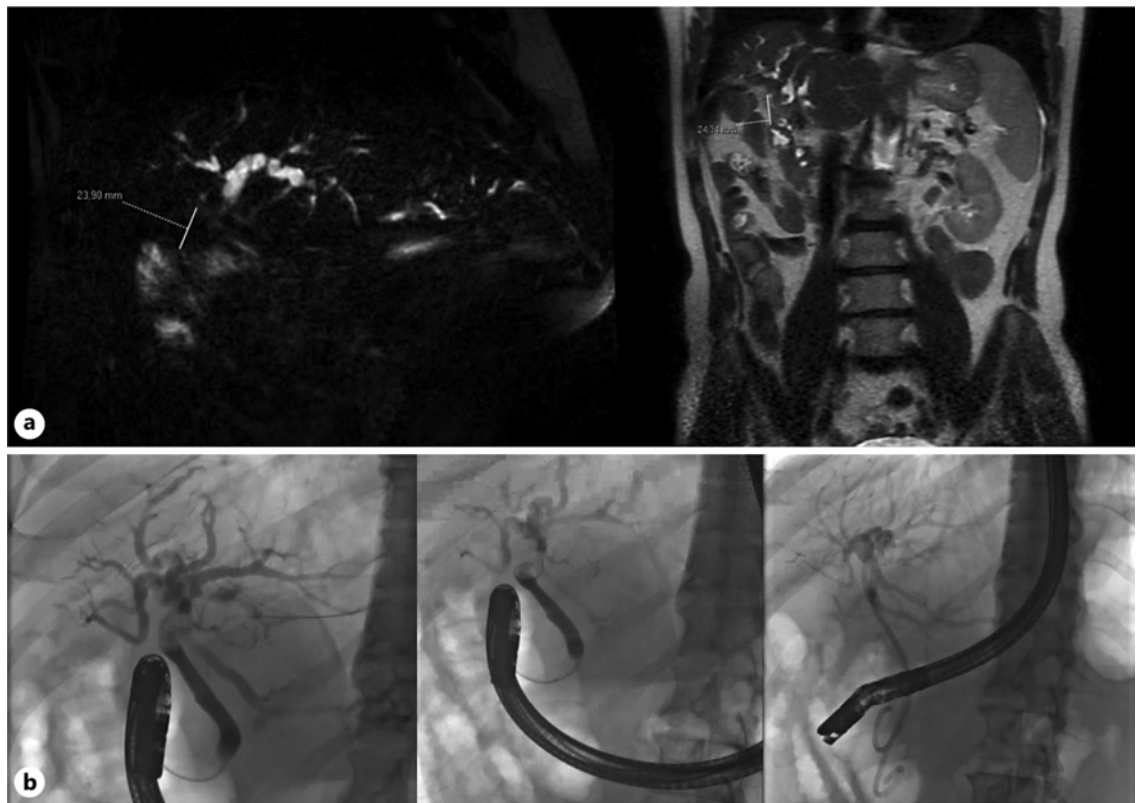


Fig. 2. a MRCP revealed a 2.4 cm intraductal lesion resulting in left hepatic duct stenosis, without parenchymal liver nodules. **b** ERCP confirmed the proximal common bile duct/left hepatic duct stenosis, and biliary drainage was accomplished with plastic stents. MRCP, magnetic resonance cholangiopancreatography.

with metastasis (Fig. 4a). Due to disease progression with evident extrahepatic involvement, the patient was no longer candidate for liver transplant and restarted chemotherapy with FOLFIRI and cetuximab.

Six months later, he was readmitted with fever, abdominal pain, and jaundice. Laboratory evaluation showed elevated inflammatory markers (white blood cells: 17.5 per microliter; C-reactive protein: 30.17 mg/dL), hyperbilirubinemia, and severe coagulopathy. Magnetic resonance cholangiopancreatography showed an infiltrating intrabiliary nodular lesion with 42 × 120 mm (Fig. 4b). A new ERCP was scheduled but given the intraductal extension of the lesion and gastric compression caused by the hypertrophied left liver lobe leading to duodenoscope mispositioning, transpapilar stents could not be deployed to overcome the bile duct stenosis (Fig. 5). During hospitalization, multiorgan dysfunction developed despite broad-spectrum antibiotic therapy. Considering the altered anatomy, EUS-BD was proposed (online suppl. Video 1; for all online suppl. material, see <https://doi.org/10.1159/000543926>). Al-

though EUS access was limited by gastric bulging, puncture of a dilated intrahepatic duct was accomplished with a 19G needle that allowed passage of a 0.035" guidewire. A 6 Fr cystotome and biliary dilators (5–8 Fr) were used for needle tract dilation. A partially covered self-expandable metal stent (GIOBOR™ 8 × 100 mm) could only be deployed under endoscopic and fluoroscopic control above the gastroesophageal junction (GEJ) with the proximal flare being incidentally deployed in a 3-cm intraparietal esophageal tract. The misplaced stent was immediately recanalized, and a stent-in-stent biliary fully covered self-expandable metal stent (WallFlex™ 80 × 10 mm) allowed hepaticoesophagostomy creation (Fig. 6). Since the stent opening was orally oriented in esophageal lumen, parenteral nutrition was started to avoid contamination. Sepsis recovering and liver test normalization were observed in a few days. In order to resume oral nutrition, a new endoscopy was performed before hospital discharge. After placement of a third stent-in-stent non-covered self-expandable metal stent (WallFlex™ 120 × 10 mm) in the hepaticoesophagostomy

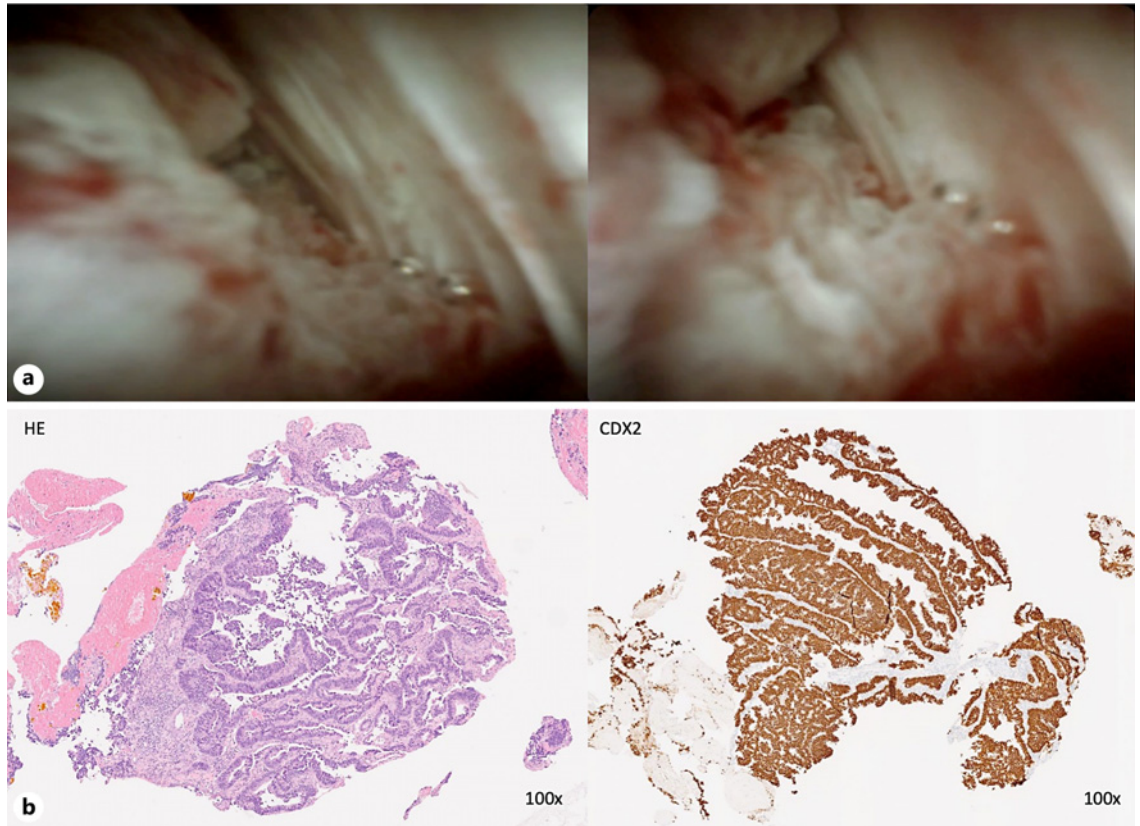


Fig. 3. a Cholangioscopy showed villous mucosa surrounded by irregular vessels suggestive of tumor neo-vascularization. **b** SpyBite™ biopsies revealed biliary metastasis, and immunohistochemistry was positive for CDX2, CK20, and SMAD4 being suggestive of colorectal origin.

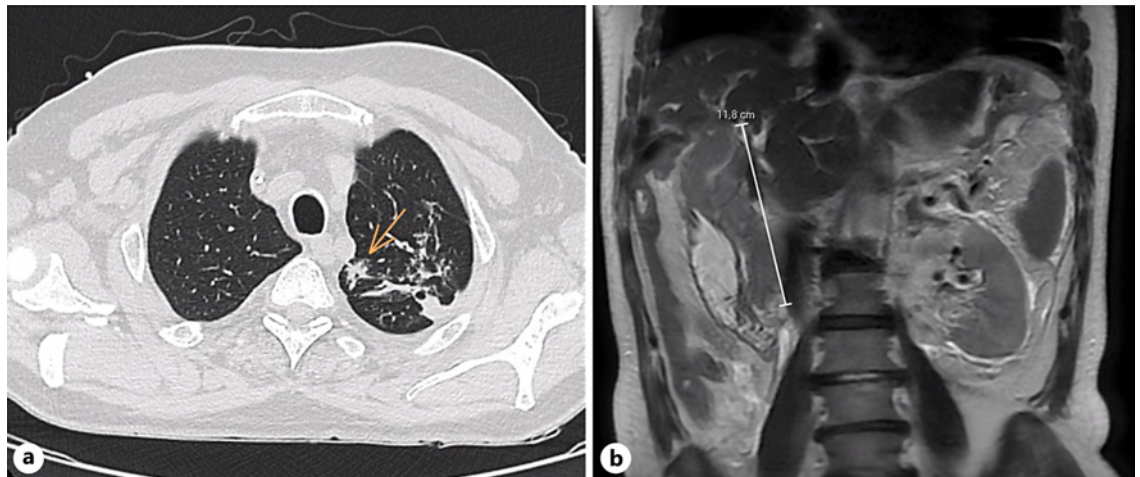


Fig. 4. a Thorax CT showing a 17-mm lung nodule suggestive of metastasis. **b** MRI showing a 120-mm diffuse infiltrating intraductal biliary lesion.

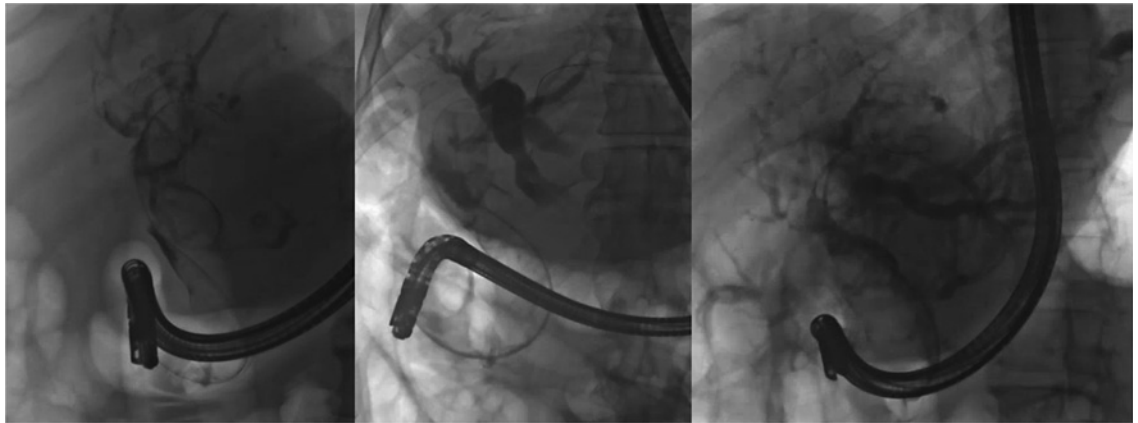


Fig. 5. ERCP was performed for biliary drainage – several nodular and pseudopolypoid defects could be observed in the cholangiography obliterating the bile duct from the hilum to the ampulla. Given the lesion extension and gastric compression by the hypertrophied liver leading to duodenoscope mispositioning, transpapilar stents could not be deployed to overcome the stenosis.

to prevent migration, the proximal flare was oriented to the stomach gently pushing with the endoscope aiding by an inflated biliary balloon (Fig. 7). The patient remained asymptomatic improving nutritional status and could resume chemotherapy. Death occurred 8 months after EUS-HES due to disease progression.

Discussion

Biliary metastasis is an extremely rare manifestation of CRC, being first reported by Herbut and Watson [11]. Differential diagnosis with primary biliary tumors, especially cholangiocarcinoma, is important for determining the treatment strategy. Biliary metastasis is typically positive for CD20/CK20 and negative for CD7/CK7 in the immunohistochemistry which suggests a colorectal origin. The mechanism of biliary metastasis from CRC may result from cancer cell implantation rather than hematogenous spread, suggesting local disease instead of systemic and highlighting the possibility of cure in an R0 resection of the common bile duct [12], even after previous liver metastasectomy. However, this is a technically demanding surgery that should only be performed in expert centers. In our patient, the lesion extension as well as the previous extensive liver surgery precluded this procedure.

Despite being an uncommon clinical condition, it seems that developing biliary metastasis is associated with poor prognosis, as reported by several authors [6, 7, 13]. These patients suffer from considerable morbidity with repeated episodes of acute cholangitis due to biliary

obstruction requiring hospitalization, antibiotic therapy, and biliary drainage, with increased complexity and consequently higher procedural risks [7], as it was observed in this case. The median survival for metastatic CRC is 30 months [5]; nevertheless, our patient presented an atypical disease course with the diagnosis of biliary metastasis 11 years after CRC and 3 years after surgery for liver metastases.

EUS-guided HGS is the procedure of choice for palliation of malignant hilar biliary obstruction after failed ERCP [8, 9, 14]. However, the initial puncture to create the HGS tract may not be technically possible in specific circumstances, such as improper bile duct alignment due to left hepatic lobe hypertrophy [15]. In this patient, gastric bulging from the hypertrophied remaining liver precluded the EUS-HGS creation and puncture was only possible above the GEJ resulting in HES. Few case reports and only one case series are published worldwide with a total number of 15 EUS-HES described in the literature to the best of our knowledge [9, 15–19]. Our patient is the only reported case of an isolated biliary metastasis from CRC submitted to EUS-HES.

EUS-HES is described as a feasible procedure, with technical success achieved in 100% of patients, and clinical success, defined as more than 50% decrease in serum total bilirubin, achieved in 90.9% [15]. However, some procedural considerations need to be outlined. Puncture site should be located within 5 cm from the GEJ at the intra-abdominal portion of the esophagus because it will minimize the risk of complications like mediastinitis. Furthermore, the self-expandable metal stent should be pushed down into the gastric lumen before fully

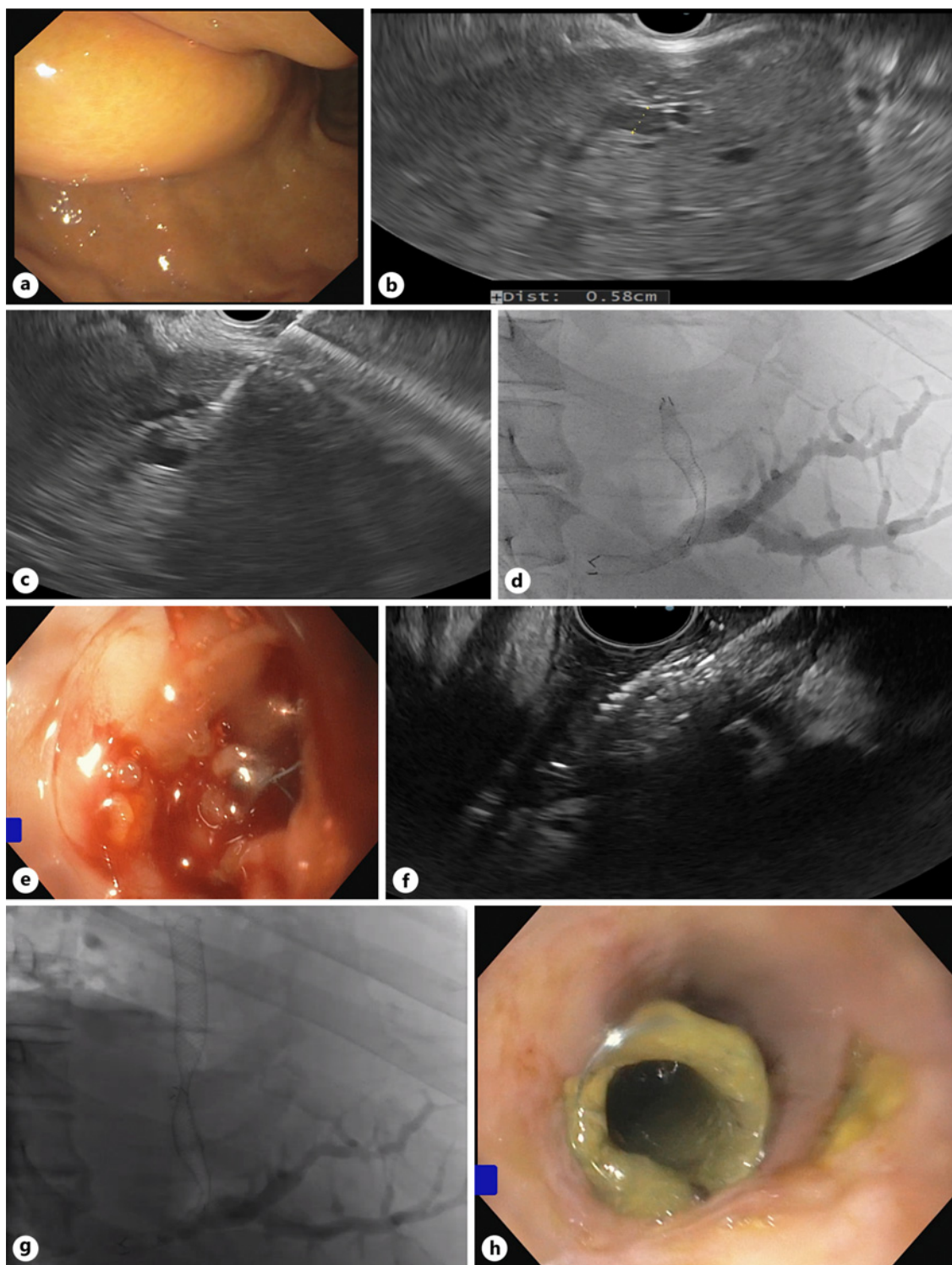


Fig. 6. **a** EUS access was limited by gastric bulging. **b** Dilated intrahepatic duct (5.8 mm). **c** Intrahepatic duct puncture with a 19G needle. **d** Partially covered SEMS (GIOBOR™ 8 × 100 mm) on fluoroscopy. **e** Proximal flare of the SEMS incidentally deployed in a 3-cm intraparietal esophageal tract. **f** The misplaced stent was recanalized through EUS. **g** Stent-in-stent FCSEMS (WallFlex™ 80 × 10 mm). **h** Hepaticoesophagostomy on endoscopy. SEMS, self-expandable metal stent; FCSEMS, fully covered self-expandable metal stent.

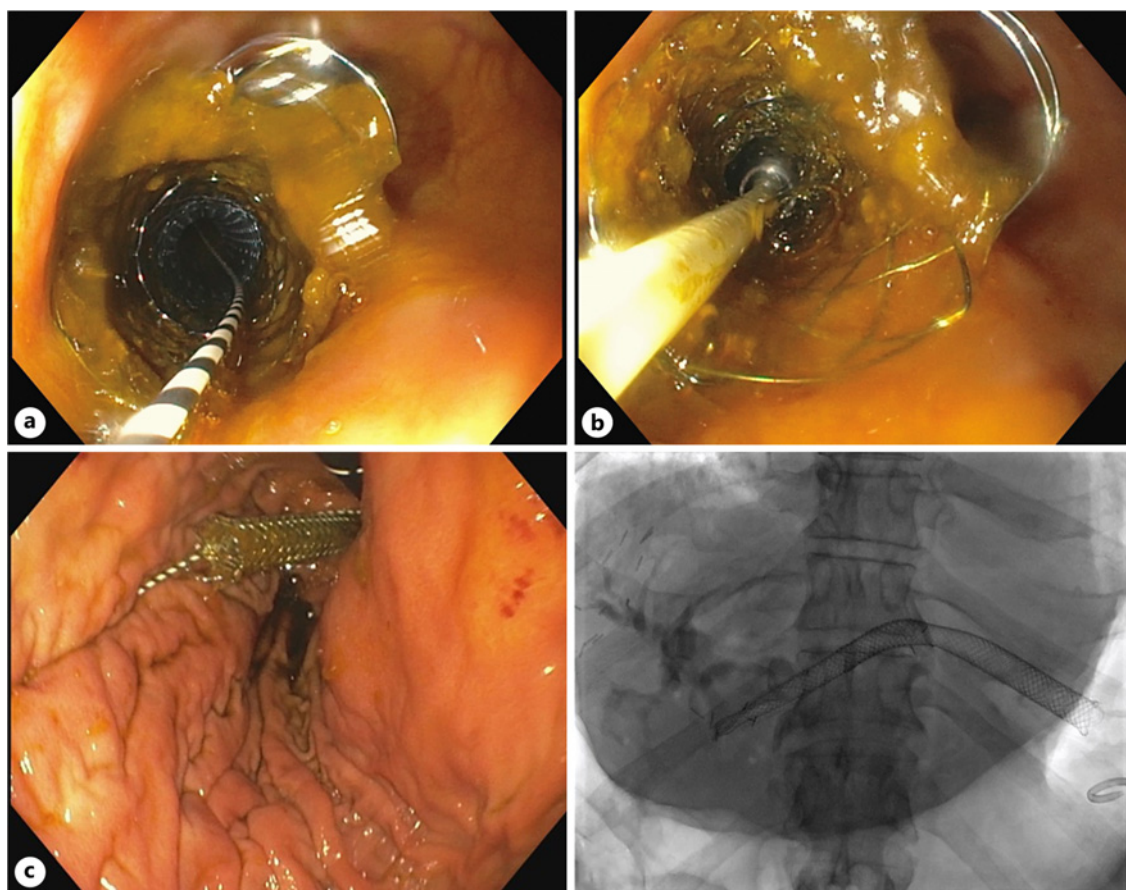


Fig. 7. **a** Placement of a third stent-in-stent NCSEMS (WallFlex™ 120 × 10 mm). **b** Inflated biliary balloon to help placing the proximal flare oriented to the stomach. **c** Proximal flare of the SEMS oriented to the stomach on endoscopy and fluoroscopy. SEMS, self-expandable metal stent. NCSEMS, non-covered self-expandable metal stent.

deployed, and this maneuver would have avoided a second endoscopy in our patient to resume oral nutrition. It is also worth mentioning the prolonged procedure time of EUS-HES when comparing with EUS-HGS (average 73 vs. 30 min [20], respectively) reflecting the higher complexity of the former. The mean overall survival is 97.8 ± 68 days [15], and our patient just died 240 days after the procedure showing a significant improved survival with good quality of life. Most of those patients die due to disease progression.

Adverse events of EUS-HES are reported in 27%, with no major procedure-related complications [15]. Stent migration was described in 2 cases and is presumably more common comparing with EUS-HGS due to higher distance between the bile ducts and the gastrointestinal lumen. Jagielski et al. [10] reported a biliopleural fistula secondary to stent migration as a serious complication of the EUS-HES managed endoscopically with stent-in-stent technique [9].

Although EUS-HES seems technically feasible, this procedure should be reserved on a case-by-case scenario in patients who fail ERCP and have an unfavorable anatomy. Due to potential risk of severe complications such as pneumothorax and mediastinitis [14], transesophageal puncture/stent placement should be avoided whenever possible. It is mandatory to ensure adequate procedural time, experienced staff, and a multidisciplinary team (interventional radiology, general surgery) as a backup in case of failed biliary drainage or in procedure-related complications. Other possible interventions, including percutaneous biliary drainage, should also be discussed with the patient according to institutional protocols and local expertise. This case highlights EUS-HES as a feasible technique in expert centers when puncture through the esophagus is inevitable, especially in patients with liver hypertrophy.

Statement of Ethics

Ethical approval was not required in accordance with local/national guidelines. The patient has given written informed consent for publication (including the publication of images).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Francisco Vara-Luiz, Ivo Mendes, and Carolina Palma wrote the manuscript. Gonçalo Nunes performed ERCP with cholangioscopy and EUS-HES stent repositioning. Marta Patita and Pedro Pinto-Marques performed EUS-guided hepaticoesophagostomy. Gonçalo Nunes and Pedro Pinto-Marques critically reviewed the manuscript. All authors approved the final version of this paper.

Data Availability Statement

The complete data of this study are not publicly available due to the patient's privacy but are available from the corresponding author upon reasonable request.