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Case Report

Early detection of biliary adenocarcinoma using probe-based confocal laser endomicroscopy: a case report

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Abstract: Background: Adenocarcinoma is the most common malignant tumor of the bile duct, originating from the mucosal epithelium. Surgical resection is typically recommended for biliary adenocarcinoma to achieve the best therapeutic outcome and prognosis. However, early detection and diagnosis remain significant global challenges. Case Presentation: This paper presents a case of a 55-year-old female patient who was admitted to the Second People's Hospital of Nanning with complaints of dull pain in the right upper abdomen for 4 months and yellowing of the skin and sclera for the past half month. The patient was diagnosed as early well-differentiated biliary adenocarcinoma by probe-based confocal laser endomicroscopy (pCLE), biliary ultrasonography, choledochoscopy and biopsy. After pancreaticoduodenectomy, exploratory laparotomy, partial bowel resection, afferent loop and efferent loop anastomosis, the patient underwent surgery successfully. After 1 year of surgical treatment, no significant postoperative complications were found in the follow-up. There was no recurrence after operation and the patient made a full recovery. Conclusion: Bile duct adenocarcinoma is a malignant tumor, and early screening, diagnosis and treatment are crucial for improving patient prognosis. In this case, early cholangiocarcinoma was detected by a combination of choledochoscopy, biliary ultrasound, and biliary confocal endoscopy. The tumor and surrounding tissues were completely removed through pancreaticoduodenectomy. The operation was successful and the patient recovered well. Confocal microendoscopy shows great promise in the early diagnosis of digestive tract diseases, owing to its high-resolution imaging capabilities and potential to detect early lesions.

Keywords: Biliary adenocarcinoma, biliary confocal endoscopy, biliary ultrasound, early diagnosis

Introduction

Biliary adenocarcinoma is a malignant tumor that arises from the extrahepatic bile duct, spanning the hilar region to the distal common bile duct. Its etiology may be associated with bile duct stones, primary sclerosing cholangitis, and other biliary diseases [1]. Globally, the incidence of cholangiocarcinoma varies significantly across regions and populations, accounting for about 3% of all digestive system tumors [2]. In China, the incidence of cholangiocarcinoma is reported to be 6 per 100,000, with an estimated 80,000 new cases annually [3]. Notably, the incidence of cholangiocarcinoma is also increasing in Western countries, especially among Hispanic and Asian populations [4]. Bile duct adenocarcinoma typically lacks specific symptoms in its early stage. Patients may present with nonspecific signs such as abdominal discomfort or pain, loss of appetite, weight loss, jaundice, and pruritus. Clinically, treatment options include surgery, radiotherapy and chemotherapy; however, the overall prognosis is not optimistic. At present, imaging examination is the primary method for preliminary diagnosis, but definitive confirmation often depends on intraoperative or postoperative pathological examination.

There are few reports on bile duct adenocarcinoma both nationally and internationally. In China, endoscopic ultrasound-guided duodenal papilla puncture, dilatation, endoscopic biliary drainage and pancreaticoduodenectomy are used for treatment. These interventions are of great significance for completely removing tumor tissue and reducing the risk of recur-

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Table 1. Main indicators of patients during diagnosis and treatment

Index	2024-02-23	2024-02-28	2024-03-06	2024-03-18	Reference interval
TB (μmol/L)	35.5	40.7	60.8	24.1	≤23.0
DB (μmol/L)	28.4	33.3	48.1	18.6	0-7
IB (μmol/L)	7.1	7.4	12.7	5.5	3.0-21.0
TP (g/L)	77.2	79.5	71.7	71.5	65-85
AIB (g/L)	42.9	44.6	40.1	40.3	40-55
GLO (g/L)	34.3	34.9	31.6	31.2	20-40
AIB/GLO	1.25	1.28	1.27	1.29	(1.2-2.4)/1
PA (mg/L)	178.0	190.0	155.5	178.0	100-400
ALT (U/L)	196.0	188	138	42.0	7-40
AST (U/L)	204.0	172.0	124	21.0	13-35
GGT (U/L)	1150.0	1191.0	1119	527	7-45
ALP (U/L)	572.0	613	603.1	377.9	50-135

Note: TB is total bilirubin; DB is direct bilirubin; IB is indirect bilirubin; TP is total protein; AIB is albumin; GLO is globulin; PA is prealbumin; ALT is alanine aminotransferase; AST is aspartate aminotransferase; GGT is gamma-glutamyl transferase; ALP is alkaline phosphatase.

rence [5]. Bile duct adenocarcinoma is a malignant tumor for which early detection and diagnosis remain global challenges. Confocal endoscopy, with its high-resolution imaging capability, shows promise in identifying early malignant changes, playing a critical role in the early diagnosis, treatment and prognosis of cholangiocarcinoma. In this case report, we describe the diagnosis and treatment of a 55-year-old female patient with cholangiocarcinoma, treated at a tertiary general hospital in Nanning, China. The surgical procedure and clinical documentation adhered to the CARE guidelines [6]. This report integrates the clinical course of the patient with insights from relevant literature.

Case presentation

A 55-year-old female patient with a history of hepatitis B for over ten years underwent regular annual follow-ups. There was no history of liver dysfunction or jaundice. She denied any chronic conditions such as hypertension or diabetes and reported no history of smoking or alcohol consumption. She also denied a history of tuberculosis and other infectious diseases. The patient presented to the Second Nanning people's Hospital on February 27, 2024 with a chief complaint of dull pain in the right upper abdomen lasting for 4 months, accompanied by yellowing of the skin and sclera for the past half month. Before admission, the patient had not received any treatment. Upon admission, she was conscious, afebrile, with a normal heart rate, and actively cooperated with the examination. Clinical manifestations included yellow urine, jaundice (yellowing of the skin and sclera), and pruritus. No rash, ecchymosis or subcutaneous hemorrhage was observed, and there were no liver palms and spider angiomas. Routine blood, stool and urine tests results were within normal limits (**Table 1**). Physical examination showed no abnormalities in the heart, kidney or abdomen. Hepatobiliary and pancreatic MRI with contrast enhancement (gadoxetic acid disodium) and magnetic resonance cholangiopancreatography (MRCP) suggested the following initial diagnoses: (1) suspected stricture at the confluence of the common bile duct and pancreatic duct; (2) intrahepatic bile duct stones; (3) gallbladder stones; and (4) liver dysfunction.

On February 28, 2024, the patient was admitted to the Department of Gastroenterology for further evaluation and treatment. Gastroscopy performed on February 29, 2024 (**Figure 1**), revealed chronic non-atrophic antral gastritis (moderate) and enlargement of the duodenal papilla. On March 5, 2024, under general anesthesia, the patient underwent endoscopic ultrasound-guided biopsy in the endoscopy room, which revealed pancreaticobiliary duct stenosis and dilatation. On March 13, 2024, the patient underwent endoscopic retrograde cholangiopancreatography (ERCP) under intravenous anesthesia and local pharyngeal anesthesia in the gastrointestinal radiography unit of the radiology department. Intraoperative proce-

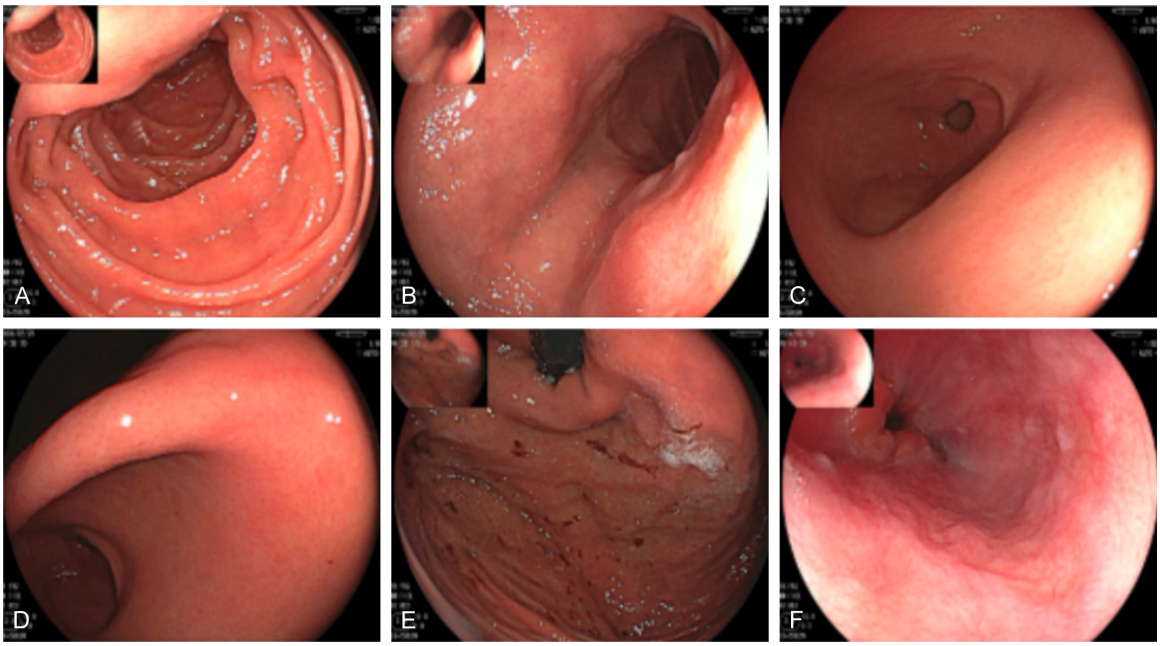

Figure 1. Gastroscopy images. A: Esophagus; B: Duodenal descending segment; C: Cardia; D: Gastric angle; E: Gastric mucosal congestion; F: Gastric mucosal congestion. Gastroscopic diagnosis: 1. Chronic non-atrophic fundal antral gastritis (moderate); 2. Duodenal papilla enlargement.

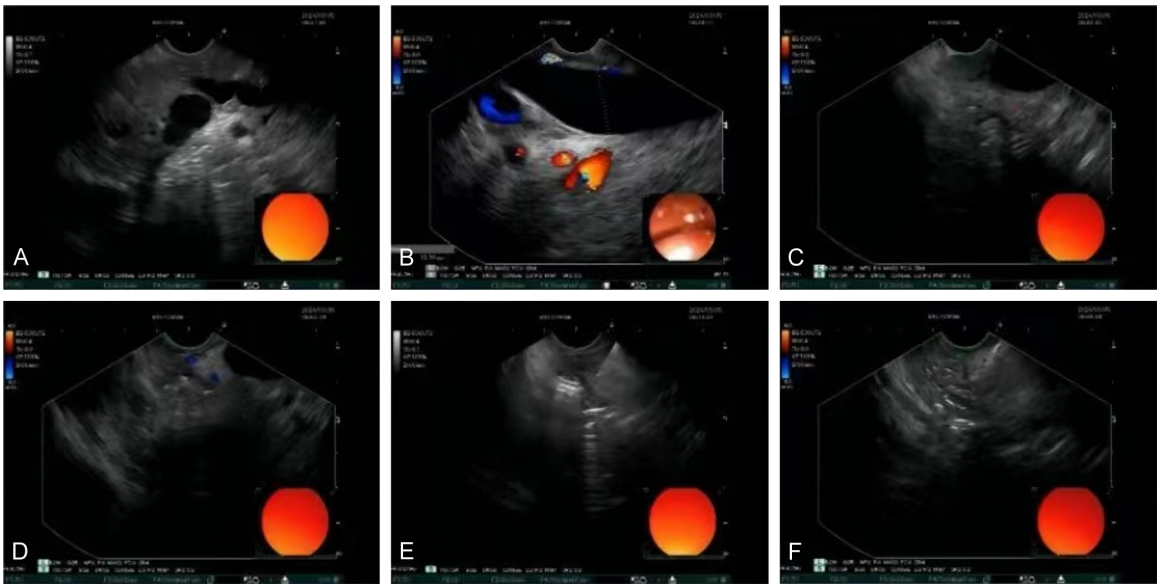

Figure 2. Endoscopic ultrasonography and ultrasound puncture images. A: Gallbladder; B: Common bile duct; C: Pancreas; D: Pancreatic head; E: Papilla echo; F: Bleeding at the puncture site. Ultrasound diagnosis: 1. Papillary inflammation and adenoma; 2. Dilatation of the common bile duct; 3. Dilatation of the main pancreatic duct.

dures included intrabiliary probe-based confocal laser endomicroscopy (pCLE), biliary ultrasonography, choledochoscopy, biopsy, endoscopic sphincterotomy (EST), endoscopic papillary dilation, endoscopic biliary drainage, stent placement, and endoscopic retrograde cholangiography (**Figures 2**, **3**). The biopsy was taken from the lesion with the most characteristic imaging features. After the operation, the patient experienced no significant discomfort and was returned to the ward. Postoperative blood work and pancreatic biochemistry tests

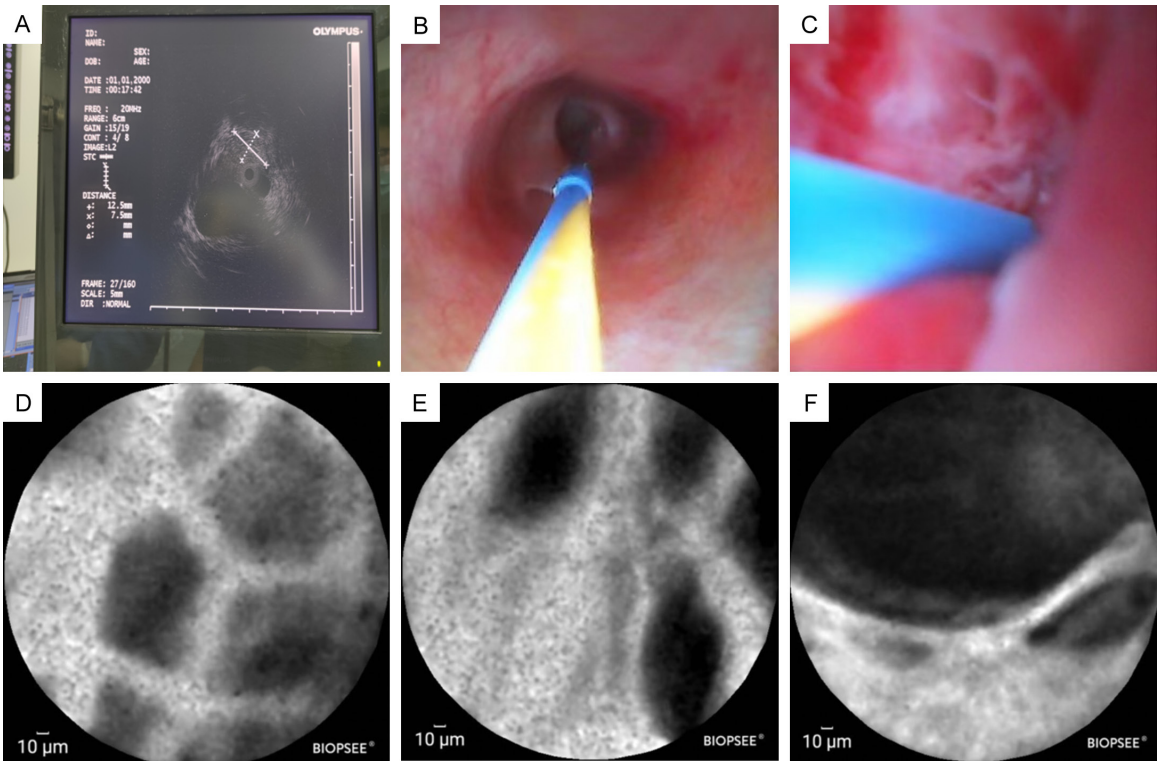

Figure 3. Bile duct opening images: endoscopic ultrasound, choledochoscopy, and biliary confocal microscopy. A: Ultrasound image of bile duct; B: Normal upper biliary tract under choledochoscopy; C: Lesions at the bile duct opening under choledochoscopy; D-F: Probe-based confocal laser endomicroscopy images. Biliary ultrasound observation showed that the middle and upper bile ducts of the common bile duct appeared clear with uniform echogenicity. The mucosa near the lower opening was significantly thickened, measuring up to 8 mm in most areas. Most of the region had slightly higher and uniform echoes, but a small area showed irregular structure. Choledochoscopy revealed obvious swelling of the mucosa near the lower segment opening of the common bile duct, with protrusions into the lumen and a tough texture; four biopsy specimens were taken. Confocal microendoscopy showed black cell clusters and irregular epithelioid structural changes in the lesions.

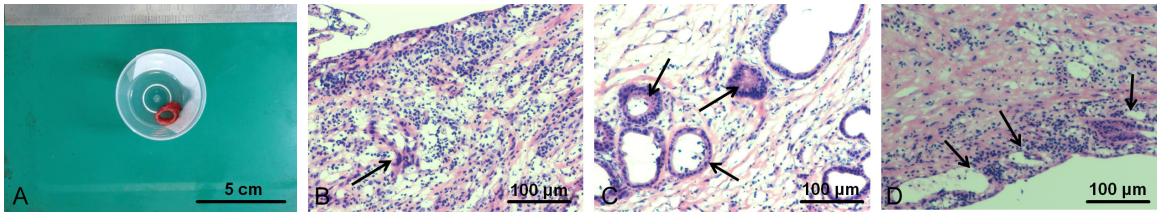

Figure 4. Intraoperative frozen pathological examination. A: Bile duct marginal tissue; B-D: Tissue network staining specimens. Pathological diagnosis: (bile duct margin) Chronic suppurative inflammation with erosion.

were reexamined, with close monitoring for pancreatitis, biliary tract hemorrhage, perforation and infection.

On March 20, 2024, the results of pathological examination revealed high-grade intraepithelial neoplasia/dysplasia (**Figures 4**, **5**). On March 26, 2024, the patient underwent pancreaticoduodenectomy, cholecystectomy, end-to-side pancreaticojejunostomy, end-to-side choledochojejunostomy, side-to-side gastrojejunostomy, and abdominal drainage. The operation was successful with satisfactory anesthesia, and intraoperative blood loss was about 200 ml. There was no blood transfusion during the operation, and the patient's vital signs were stable during the operation. After recovering from anesthesia, the patient was transferred back to the ward. Postoperative management included active infection prevention, acid and enzyme inhibition, adequate drainage, nutritional support and other supportive treat-

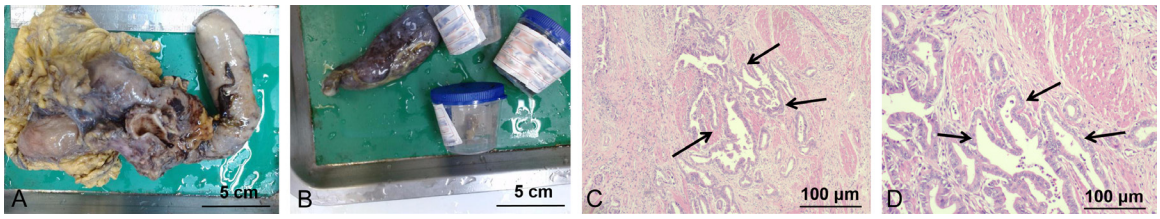

Figure 5. Postoperative pathological examination. A, B: Pancreaticoduodenal and common bile duct, gallbladder, lymph nodes; C, D: Tissue staining specimens. Pathological diagnosis: highly differentiated bile duct adenocarcinoma, maximum diameter of the tumor approximately 2 cm, involving the duodenal submucous muscle layer, with no obvious nerve and vascular invasion and no tumor thrombus.

ments. No complications such as pancreaticojejunal or choledochojejunal anastomotic leakage occurred, and the short-term prognosis was favorable.

On April 8, 2024, the patient developed abdominal distension and pain with a palpable mass detected in the left lower abdomen. Ultrasound of the subcutaneous tumor revealed dilation from the ascending colon to descending colon. Enhanced CT of the upper abdomen showed (1) pancreatic and duodenal postoperative changes; (2) new small bowel obstruction; and (3) common hepatic duct wall thickening, suggestive of inflammatory lesions. On April 10, 2024, the patient underwent laparotomy, intestinal adhesion release, and bowel repositioning. The operation was successful with satisfactory anesthesia, the intraoperative blood loss was approximately 50 ml, and no blood transfusion was required. The vital signs were stable during the operation. After anesthesia recovery, the patients were safely transferred back to the ward. Postoperative management included active prevention of infection, gastric protection, adequate drainage, promotion of gastrointestinal motility, and nutritional support. There were no postoperative complications such as bleeding, intra-abdominal gastrointestinal re-adhesion or obstruction, and the prognosis was favorable.

Discussions

Long-standing gallstones can cause biliary inflammation and recurrent infections, thereby promoting abnormal proliferation of local cells and increasing the risk of cholangiocarcinoma. However, the early diagnosis of cholangiocarcinoma remains a major clinical challenge [7]. Based on the clinical manifestations of the patient (yellow urine, jaundice, and pruritus) and MRI findings, an initial diagnosis of stenosis at the confluence of the common bile duct and pancreatic duct, along with intrahepatic bile duct stones, was made. Stone removal was subsequently performed. To evaluate whether intrahepatic bile duct stones had caused malignant transformation, the patient underwent gastroscopy, endoscopic ultrasonography, biliary ultrasound, pCLE and other auxiliary examinations. A final diagnosis of biliary adenocarcinoma was established based on combined imaging and pathological findings. Given that surgery remains the only curative option for biliary adenocarcinoma, the principle of R0 resection should be upheld when surgical indications are met and informed consent is obtained. In this case, the patient underwent pancreaticoduodenectomy, exploratory laparotomy, partial bowel resection, and afferent loop and efferent loop anastomosis for this patient. The surgical objective was to achieve complete tumor resection while preserving normal tissue and function to the greatest extent possible. Postoperative pathology confirmed a diagnosis of well-differentiated bile duct adenocarcinoma. After a series of treatments, the patient recovered well and was successfully discharged. During one year of follow-up, no obvious postoperative complications, tumor recurrence, or metastasis were observed. The prognosis of patients with cholangiocarcinoma is affected by multiple factors. Early diagnosis, multidisciplinary comprehensive treatment and individualized postoperative management are critical for improving the prognosis. Clinically, regular screening, accurate diagnosis and comprehensive treatment, combined with patient education and psychological support, can significantly enhance both survival rates and quality of life for patients.

The patient had a history of hepatitis B for more than ten years. Hepatitis B virus infection is

one of the risk factors for biliary adenocarcinoma, as prolonged infection can lead to chronic hepatitis, cirrhosis, and an increased risk of malignant transformation in the biliary system. pCLE is an advanced endoscopic technique that provides high-resolution images of biliary mucosal cells and subcellular levels in real time. It can not only clearly show the cytological characteristics of biliary mucosa, but also help distinguish between inflammation, benign stenosis and precancerous lesions and early malignant transformation of biliary adenocarcinoma. For patients with hepatitis B, this technique is particularly important in detecting minimal biliary lesions, which is helpful for early diagnosis and precise treatment. In addition, the abnormal elevations in total bilirubin (TB), direct bilirubin (DB), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), and alkaline phosphatase (ALP) provide important clues for the diagnosis of biliary adenocarcinoma, as well as key reference for evaluating therapeutic effects and subsequent management. After treatment, the levels of TB, DB, ALT, GGT and ALP were significantly decreased, indicating clinical improvement.

The strength of this case lies in the timely implementation of early screening and diagnosis, which is crucial for the surgical outcome and prognosis of patients with cholangiocarcinoma. Additionally, pCLE technology plays a key role in improving the diagnostic accuracy of cholangiocarcinoma. Compared with traditional imaging techniques, pCLE provides higher-resolution real-time histopathological imaging, which helps reduce misdiagnosis and missed diagnosis, thereby ensuring timely and accurate treatment. However, a limitation of this case is that the diagnostic accuracy of pCLE is highly dependent on the operator's experience and skill, leading to potential inter-operator variability. This presents challenges for the widespread adoption and standardization of technology. Moreover, pCLE technology requires specialized equipment and training, which may be a limiting factor in resource-constrained settings.

This case offers valuable insights and implications. Despite ongoing advancements in imaging technologies, there are still limitations in the diagnosis of bile duct malignant tumors. As an emerging endoscopic imaging technology, pCLE presents a promising approach for distinguishing benign and malignant biliary strictures [8]. Koda et al. [9] improved the sensitivity and negative predictive value of pCLE in the diagnosis of biliary malignant tumors by Miami classification. However, the diagnosis of cholangiocarcinoma in Guangxi, China remains challenging, with many patients missing the optimal window for surgical intervention by the time of diagnosis. As the first medical institution to perform ERCP in Guangxi, the Department of Gastroenterology of our hospital also pioneered the introduction of confocal endomicroscopy, applying it for the early screening of biliary tract cancers. This initiative has yielded remarkable results and effectively addressed diagnostic challenges. The procedure outcomes were favorable, and the patient recovered smoothly. These findings underscore the advantage of pCLE in detecting early-stage biliary diseases. Early screening, accurate diagnosis and timely treatment are essential for improving the prognosis of patients with biliary tract diseases, such as cholangiocarcinoma, cancer, biliary adenocarcinoma or biliary stricture.

Although bile duct adenocarcinoma is the predominant pathological type, its relatively low incidence and mostly sporadic occurrence have resulted in relatively few clinical reports. In addition, numerous challenges in the diagnosis and treatment of biliary adenocarcinoma have contributed to the limited systematic research and case reporting. Hoti et al. [10] reported a case of 51-year-old man with biliary adenoma who recovered well after surgical treatment. Yoo et al. [11] reported a case of 67-year-old man who was diagnosed with jaundice. Imaging revealed a mass involving the common hepatic duct and common bile duct. Pancreatoduodenectomy was performed, and the pathology showed both squamous cell carcinoma and adenocarcinoma. Liver metastasis occurred 3 months later, and the patient died 8 months postoperatively. It can be seen that radical resection is the only chance for long-term survival. However, the lack of early screening and diagnosis often leads to poor prognosis. Notably, pCLE demonstrates high accuracy in diagnosing malignant cholangiocarcinoma [12]. A study showed that the sensitivity, specificity, positive predictive value and negative predictive value of pCLE in detecting malignant tumors were 98%, 67%, 71% and 97%, respec-

tively, outperforming histopathological sampling, which had corresponding values of 45%, 100%, 100% and 69% [13]. The combination of ERCP and pCLE increased the sensitivity to 89%, specificity to 71%, and accuracy to 82%. When histopathology, ERCP and pCLE were combined, sensitivity remained at 89%, while specificity and the accuracy improved to 88% [14]. Moreover, studies have shown that in patients with uncertain biliary strictures, the sensitivity and accuracy of cytology combined with pCLE in the diagnosis of malignant strictures are similar to those of choledochoscopy, and pCLE facilitates real-time histopathological examination of biliary strictures [15]. Therefore, as an emerging diagnostic tool, pCLE holds great potential and promising applications in the diagnosis of cholangiocarcinoma.

Conclusion

The early symptoms of cholangiocarcinoma closely resemble those of bile duct stones and gallbladder stones, making early differential diagnosis more challenging. pCLE can accurately diagnose bile duct tumors. This technology offers high imaging clarity and sensitive detection of early pathological changes, with vast potential for application in both diagnostic research and clinical practice for biliary tract diseases. This technology can reveal the microstructure of the digestive tract mucosa, enabling early detection and treatment, and may become a key area of focus in future digestive tract medicine research.

Disclosure of conflict of interest

None.

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