

Endoscopic ultrasonography confirmed recurrence of gallbladder cancer: a case report (with a video).

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Abstract

Biliary tract cancer is the most common biliary malignant tumor, which is considered to be a high-grade malignant tumor because of its frequent recurrence / metastasis[1]. Late recurrence of gallbladder cancer after operation is rare. We presented a case of recurrent cancer after radical resection of gallbladder cancer.

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Abstract

Biliary tract cancer is the most common biliary malignant tumor, which is considered to be a high-grade malignant tumor because of its frequent recurrence / metastasis[1]. Late recurrence of gallbladder cancer after operation is rare. We presented a case of recurrent cancer after radical resection of gallbladder cancer.

Key words: Recurrence of gallbladder cancer, diagnosis, endoscopic ultrasonography (EUS)

Case presentation

A 63-year-old man was admitted to hospital 12 years ago because of right upper abdominal pain for 2 weeks. B-ultrasound revealed a hypoechoic mass at the bottom of the gallbladder. CT indicated that the gallbladder wall was linearly enhanced, the inferior gallbladder wall thickened, and the lesion was linearly strengthened, with a size of about 14 × 13 mm. In consideration of gallbladder cancer, radical cholecystectomy was performed after evaluation of lymph node and systemic condition, without met-astasis or other surgical taboos. The postoperative pathology suggested that the adenocarcinoma was accompanied with atypical hyperplasia, and the cutting end was not reached. Then gemcitabine combined with oxaliplatin was given six times of chemotherapy. During the first three years after operation, no significant abnormalities were

found in liver function, CA199, CEA and other tumor indicators as well as enhanced CT of abdomen and pelvis, which were reviewed every 3-6 months. In the course of 3-9 years after operation, the results of chest, abdomen and pelvis enhanced CT or MRI, were normal every other year. As of December 2019, abdominal MRI showed that part of the intrahepatic bile duct was slightly dilated, and the extrahepatic bile duct in the portal area was slightly dilated, about 13mm in width, and there was no obvious filling defect in the cavity. However, no further examination was carried out at that time. In September 2020, the patient went to the doctor again due to fatigue, and the CA199 rose to more than 5 times of the normal upper limit. Abdominal enhanced CT suggested intrahepatic bile duct dilatation, left hepatic duct nodule (Figure1 B-C), abdominal MRI suggested partial intrahepatic bile duct dilatation, portal bile duct dilatation, and no clear filling defect was found in the duct system (Figure1 A). Further improvement of endoscopic ultrasonography(EUS) suggested that the hypoechoic space in the confluence area of the left and right hepatic ducts of the hilar bile duct (considering it's a cancer) was accompanied by dilatation of the upstream bile duct and a small piece of hyperechoic shadow could be seen in the focus, which may be the nodal shadow of the surgical line(Figure2 A-B). According to the previous medical history and related examination, clinicians considered the recurrence of gallbladder cancer after operation, and considered that the focus was small and EUS-FNA had the risk of needle metastasis. Finally, no puncture examination was performed and surgical resection was planned. Bileductectomy was performed after the evaluation of the whole body, and a faint line knot was seen during the operation, which was further confirmed as a recurrence after the operation (Figure3 A and Video). The frozen rapid pathology showed that the cutting edge of the lower segment of the bile duct was positive, so the surgical method was changed to radical pancreaticoduodenectomy. Postoperative pathology showed highly differentiated adenocarcinoma, vascular invasion, negative incisional margin and no lymph node metastasis (Figure3 B-C). After the operation, the patient was sent to the intensive care unit.

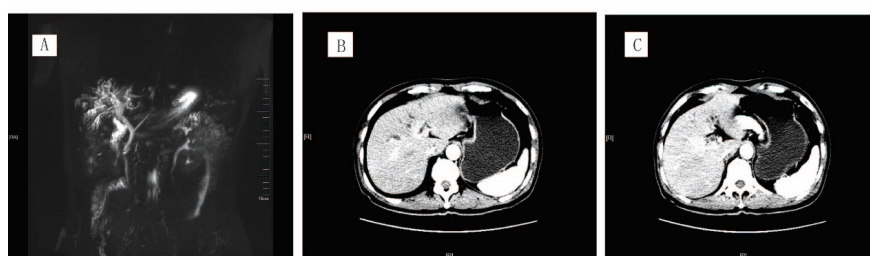


Figure1 A: Part of the intrahepatic bile duct was dilated in MRI, the bile duct in the portal area was dilated, the width was 14mm, and the diameter of the lower duct was slightly narrow. there was no clear filling defect in the duct system shown. B: Intrahepatic bile duct dilatation could be seen on CT.C: There seemed to be a low density focus at the confluence of left and right bile duct.

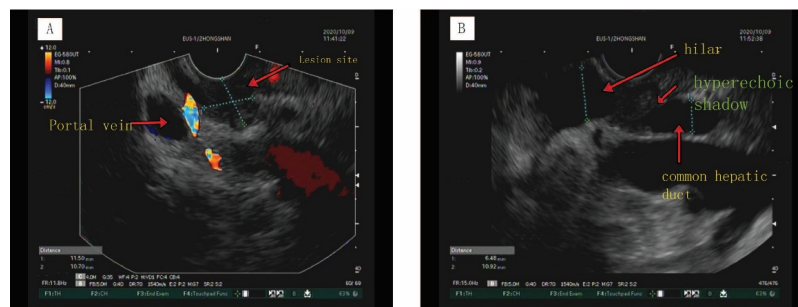


Figure2 A:A mass of hypoechoic lesions could be seen at the confluence of the left and right hepatic ducts, with a cross-sectional area of 10.5x11.7mm.B:The upstream bile duct of the lesion was dilated for 11mm, and the common hepatic duct was 6.5mm. A small piece of hyperechoic shadow might be the nodal shadow of the surgical line.

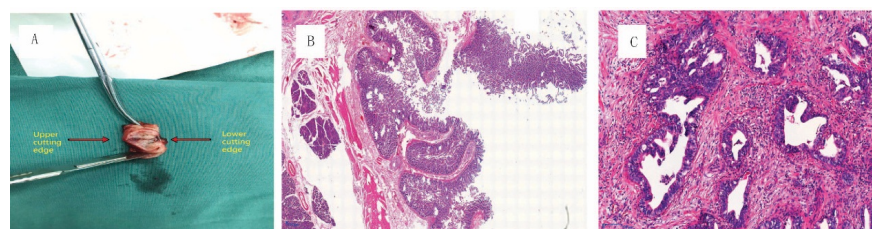


Figure3 A:The lower incisal margin of the gross specimen seen in cholecystectomy is suspected to be incomplete. B:Histological pathology of cholangiocarcinoma (hematoxylin staining 20X): normal pancreatic tissue in the lower left corner and highly differentiated glandular duct in the middle. C:Histological pathology of cholangiocarcinoma (hematoxylin staining 100X): the nucleus of cholangiocarcinoma was deeply stained and disordered.

Discussion

Gallbladder carcinoma is one of the most common and invasive malignant tumors in the biliary system with poor prognosis. Tumor-free margin is one of the most important predictors of survival in early gallbladder cancer, but it is reported that up to 61% of cases will develop residual disease (RD), after resection, which is related to the low disease specific survival rate[2,3]. Many surgeons believe that patients who survive disease-free within 5 years can be cured and then stop active follow-up [4]. However, it is not uncommon for patients with various cancers to relapse after long-term remission. In this paper, 12 years after radical resection of gallbladder cancer, the patient had recurrent cancer at the surgical incision, which may be related to cancer dormancy, that is dormant tumor cells spread from dormancy to proliferation due to some regulatory mechanisms, forming a part of tumor progression. In addition, the metastatic growth of diffuse tumor cell (DTC) in primary tumors may be the cause of metastatic diseases several years or even decades after successful surgical and adjuvant treatment of primary tumors [5].

The recurrence of gallbladder cancer is located in the surgical incision of the bile duct, the onset of hidden, not easy to enter the anatomical position, also not easy to be found, the first choice for treatment is surgery. Preoperative imaging methods including transabdominal ultrasound, CT and magnetic resonance imaging (MRI) can show bile duct tumors and predict varying degrees of unresectability. The combination of brush

cytology and intraductal biopsy during ERCP is the standard method for diagnosis, with high specificity but low sensitivity, mostly between 35% and 70% [6].

Due to the inherent limitations of endoscopic bile duct sampling, EUS is increasingly used in the diagnosis and staging of biliary tract cancer. EUS has a unique advantage because the ultrasonic probe is inserted into the stomach to observe the biliary tract and liver, thus reducing the distance between the probe and the lesion. Cancer of the biliary tract usually presents as a hypoechoic mass with blurred boundaries. In terms of image recognition and non-FNA recognition, EUS identified 156 (96%) of 162 stenoses or tumors [7]. In the study of reported cholangiocarcinoma patients, the detection rate of EUS images in 76 of 81 cases (94%) was better than that of CT (23 of 75 cases [30%]; $P < 0.001$) and MRI examination (11 cases of tumors were found in 26 patients [42%]; $P=0.07$) [6].

In the study of Mohamadnejad M et al[9], it was found that the overall sensitivity of EUS-FNA in the diagnosis of adenocarcinoma was 73%. In distal tumors, the sensitivity of EUS-FNA to tissue diagnosis was 81%, while that of proximal tumors was 59%. This can be explained by the fact that the intrapancreatic part of the bile duct is more easily visible from the duodenal bulb, while the bile duct near the hilum runs closer to the liver and away from the duodenum and gastric cavity. The EUS imaging quality decreases with the increase of distance, and the FNA accuracy of the imaging target decreases. The practicability of primary tumor EUS FNA after negative or unsuccessful ERCP sampling is supported by studies, which show that the sensitivity in this case is 77% and 89% respectively[7,8]. The sensitivity of EUS in detecting the unresectability of cholangiocarcinoma is 53%, and the specificity is 97%. It is a supplement to the detection of unresectability of cholangiocarcinoma by CT or magnetic resonance imaging[8].

However, tumor seeding has been reported in many sites after EUS or CT-guided fine needle aspiration biopsy ((FNA)). It is reported that the risk of clinically significant tumor implantation after FNA is 1/10000-40000 [9]. Although the main diagnostic method of EUS is FNA, fine needle aspiration of (FNA) for EUS of primary tumors is not recommended. For some patients who are careful to exclude other benign lesions for surgical treatment, we do not recommend FNA.

Although some patients have stents, there is still no need to worry about the impact of EUS imaging. It is generally overcome by imaging from different locations, minimizing the injection of air that usually enters the catheter through the stent, or the initial removal of the stent. In addition, it should be noted that some primary sclerosing cholangitis (PSC) patients are often accompanied by multiple bile duct strictures, more obvious connective tissue hyperplasia and diffuse benign lymphadenopathy. These features hinder EUS imaging and FNA.

Among the tumor markers, although the specificity of CA199 is not high, it has a high sensitivity of 71.7%, and with the progress of clinical stage, its sensitivity increases, which is a predictor of the therapeutic effect and prognosis of gallbladder cancer [10]. During the follow-up period, we should be aware of the possibility of tumor recurrence and metastasis when we encounter the increase of CA199.

AUTHOR CONTRIBUTIONS

XL: involved in study design, literature research, clinical studies, data acquisition, data analysis/interpretation, manuscript preparation, manuscript editing.

HD: was guarantor of integrity of entire study, involved in study concepts, manuscript revision/review, manuscript final version approval.

CONSENT STATEMENT

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understand that his name and initials will not be published and due efforts will be made to conceal their identity.

CONFLICT OF INTEREST

There are no conflicts of interest. The manuscript has been read and approved by all the authors.

DATA AVAILABILITY STATEMENT

No additional data available.

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References

1. Kijima H, Wu Y, Yosizawa T, Suzuki T, Tsugeno Y, et al. (2014) Pathological characteristics of early to advanced gallbladder carcinoma and extrahepatic cholangiocarcinoma. *Journal of Hepato-Biliary-Pancreatic Sciences*.21(7): 453-458.
2. Choi KS, Choi KB, Park P, Kim WB, Choi SY.(2015) Clinical characteristics of incidental or unsuspected gallbladder cancers diagnosed during or after cholecystectomy: a systematic review and meta-analysis. *World journal of gastroenterology*.21: 1315-1323.
3. Vinuela E, Vega EA, Yamashita S, Sanhueza M, Mege R, et al.(2017) Incidental gallbladder cancer: residual cancer discovered at oncologic extended resection determines outcome: a report from high- and low- incidence countries. *Ann Surg Oncol* .24: 2334-2343.
4. Araida T, Higuchi R, Hamano M, Kodera Y, Takeshita N, et al. (2009) Hepatic resection in 485 R0 pT2 and pT3 cases of advanced carcinoma of the gallbladder: results of a Japanese Society of Biliary Surgery survey A multicenter study. *Journal of hepato-biliary-pancreatic sciences*.16: 204-215.
5. Páez D, Labonte MJ, Bohanes P, Wu Z, Benhanim L, et al.(2012) Cancer dormancy: A model of early dissemination and late cancer recurrence. *Clinical Cancer Research*.18(3): 645-653.
6. Ro"sch T, Hofrichter K, Frimberger E, Meining A. (2004) ERCP or EUS for tissue diagnosis of biliary strictures_A prospective comparative study. *Gastrointestinal endoscopy*.60: 390-396.
7. Fritscher-Ravens A, Broering DC, Knoefel WT, Rogiers X, Swain P, et al. (2003) EUS-guided fine-needle aspiration of suspected hilar cholangiocarcinoma in potentially operable patients with negative brush cytology. *American journal of gastroenterology*.99: 45-51.
8. Mohamadnejad M, DeWitt JM, Sherman S, LeBlanc JK, Pitt HA. et al. (2011) Role of EUS for preoperative evaluation of cholangiocarcinoma: a large single-center experience. *Gastrointestinal Endoscopy*.73(1): 71-78.
9. Smith EH(1991) Complications of percutaneous abdominal fine-needle biopsy. *Radiology*. 178: 253-258.
10. Wang YF, Feng FL, Zhao XH, Ye ZX, Zeng HP, et al. (2014) Combined detection tumor markers for diagnosis and prognosis of gallbladder cancer. *World journal of gastroenterology*. 20(14): 4085-92.

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