Peroral cholangioscopy–guided probe-based confocal laser endomicroscopy for preoperative diagnosis of pancreatic cancer in a patient with surgically altered anatomy

Yuki Tanisaka, MD, PhD,[1] Shomei Ryozawa, MD, PhD,[1] Kouichi Nonaka, MD, PhD,[1] Shinichi Ban, MD, PhD,[2] Akashi Fujita, MD[1]

A 79-year-old man was referred to our hospital because of jaundice. He had previously undergone Billroth-II gastrectomy for gastric cancer. Contrast CT showed a mass lesion in the pancreatic head with contrast effects and invasion of the distal bile ducts (Fig. 1). Additionally, ERCP was performed to obtain more detail.

Because of the patient's prior gastrectomy, ERCP was performed with a short-type single-balloon enteroscope, SIF-H290S (Olympus Medical Systems, Tokyo, Japan) with a working length of 152 cm and channel diameter of 3.2 mm. Cholangiography showed a defect in the distal bile duct (Fig. 2). The procedure was then completed with fluoroscopy-guided biopsy of the bile duct. However, the size of the biopsy sample was insufficient to enable a conclusive diagnosis.

ERCP was performed again 2 weeks later (Video 1, available online at www.VideoGIE.org). With the aim of improving diagnostic ability, a CF-H260AI colonoscope (Olympus Medical Systems Corporation, Tokyo, Japan) with a working length of 133 cm and channel diameter of 3.7 mm was used to perform peroral cholangioscopy (POCS) guided by SpyGlass DS (Boston Scientific Corp, Marlborough, Mass, USA) fluorescein-dripping probe-based confocal laser endomicroscopy (pCLE)[1,2] (CholangioFlex, Cellvizio; Mauna Kea Technologies, Inc, Paris, France) and POCS-guided biopsy.

When the papilla was reached, it was possible to insert the cholangioscope inside the bile duct. Both findings suggested cancer, with POCS showing an irregular, hemorrhagic, papillary protrusion lesion, and pCLE showing a dark ductal structure with irregular margins (Fig. 3A-C). POCS confirmed that the bile ducts at nonlesion sites had normal mucosa, and pCLE showed a reticular network of thin, dark, branching bands,[3,4] considered to be normal (Fig. 4A-C). POCS-guided biopsies were performed at both lesion and nonlesion sites.

In contrast to the initial fluoroscopy-guided biopsy performed with ERCP (Fig. 5A, B), a sample of sufficient size was collected by the POCS-guided biopsy. The biopsy samples contained atypical cells with hyperchromatic nuclei and eosinophilic cytoplasm. Similarly to the pCLE findings, these formed a ductal structure with irregular margins.

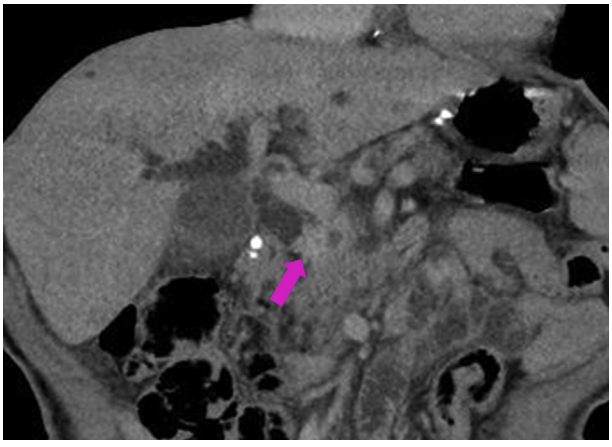

Figure 1. Contrast CT of the abdomen showing a mass with contrast effects in the distal bile duct *(pink arrow)*.

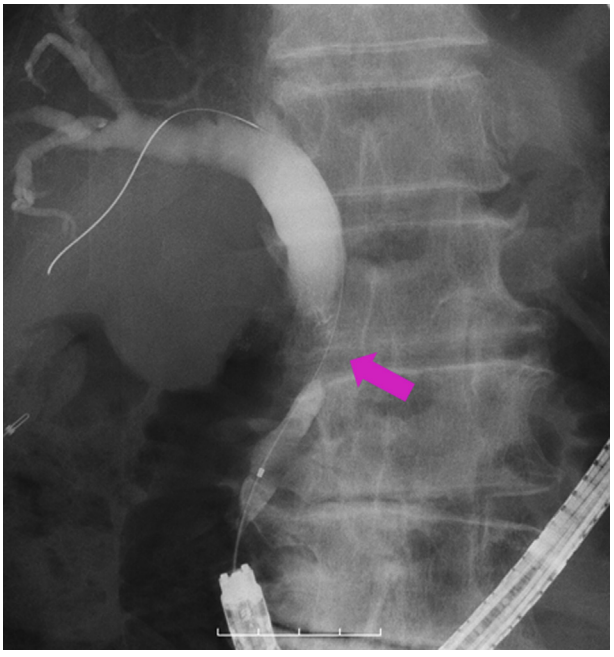

Figure 2. Cholangiographic view of the lesion showing a defect in the distal bile duct *(pink arrow)*.

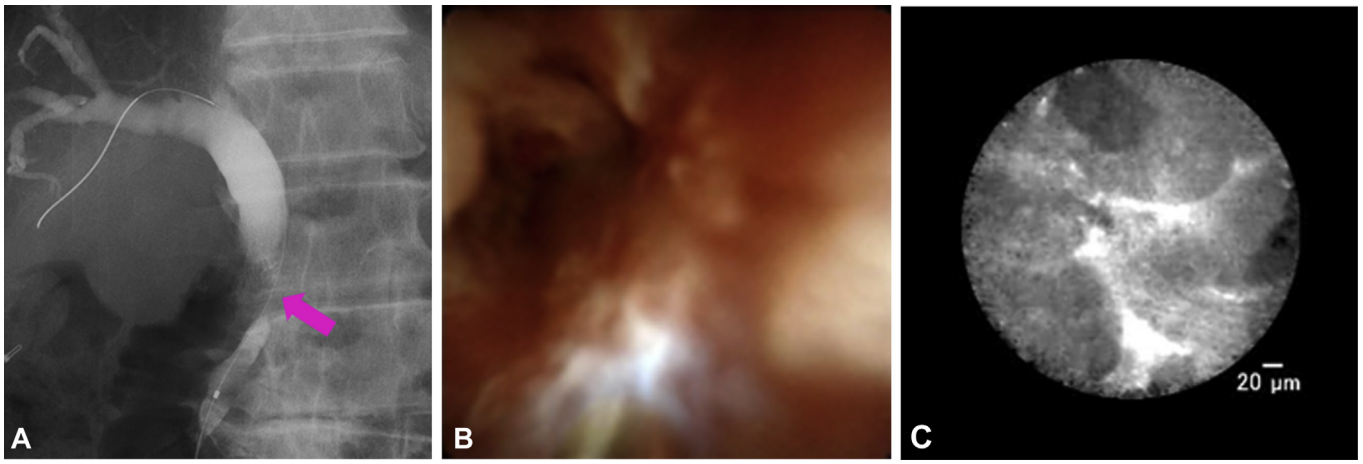

Figure 3. A, Cholangiography showed the lesion (*pink arrow*). **B**, Peroral cholangioscopy showed irregular, hemorragic, papillary projection. **C**, pCLE showed a dark ductal structure with irregular margins, so cancer was suspected.

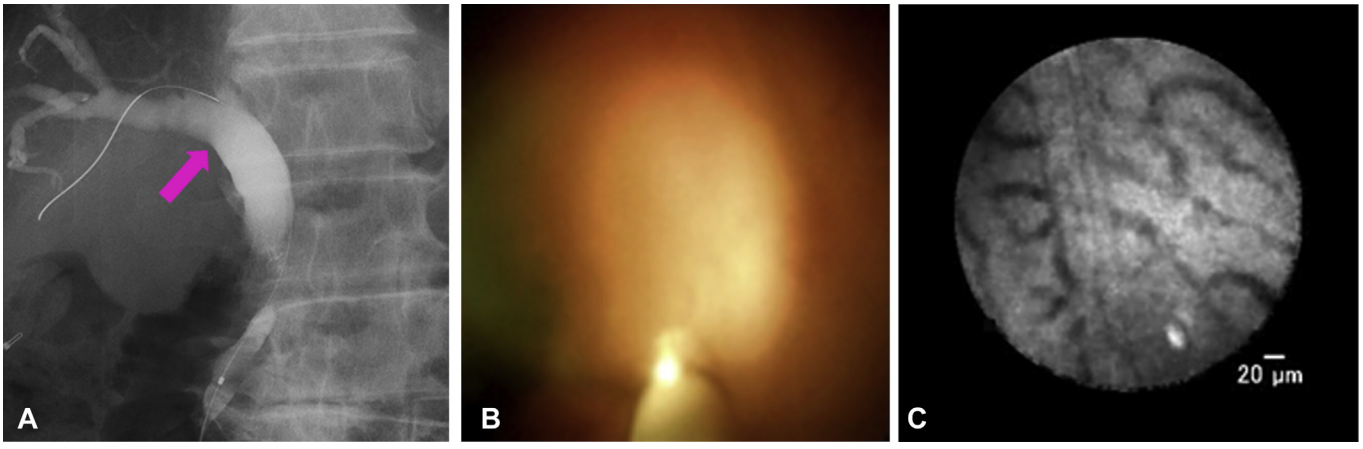

Figure 4. A, The part of nonlesion site (*pink arrow*). **B**, The mucosa was seen to be normal. **C**, pCLE showed a reticular network of thin, dark, branching bands.

The nuclei showed marked variations in size, irregular morphology, and irregular arrangement, indicating adenocarcinoma (Fig. 5C, D).

Biopsy specimens from normal bile ducts showed no malignancy. Therefore, a preoperative diagnosis of pancreatic cancer was made, and pancreatoduodenectomy was performed. The histopathologic findings from the surgical samples were similar to those from the POCS biopsy tissue samples, and irregular, invasive proliferation by atypical bile ducts with eosinophilic cytoplasm was found, confirming pancreatic cancer (Fig. 6A, B).

In patients with Billroth-II gastrectomy, it is common to use a forward-viewing endoscope like the single-balloon enteroscope we used initially in this case.[5] The absence of an elevator makes adjusting angles on devices difficult, and in the present case, this restriction resulted in an insufficient biopsy sample size. However, POCS enabled angle adjustment of the cholangioscope itself inside the bile duct, which was highly effective for pCLE and biopsy. In fact, exact pCLE findings were possible with this method, and we were able to obtain a sufficiently large biopsy sample by POCS-guided biopsy.

Sensitivity and specificity for malignancy based on visual findings of cholangioscopy were 90% and 95.8%, respectively,[6] although accuracy for the combination of ERCP and pCLE was significantly higher in comparison with ERCP and tissue acquisition (90% vs 73%; $P = .001$).[4] Furthermore, a prospective multicenter international study showed that pCLE provided a more accurate and sensitive diagnosis of cholangiocarcinoma than did tissue sampling alone.[7] Although the neoplastic changes were seen on cholangioscopy alone in this case, pCLE is more reliable because real-time microscopic images of the bile duct tissue are seen and can be expected to increase the accuracy.

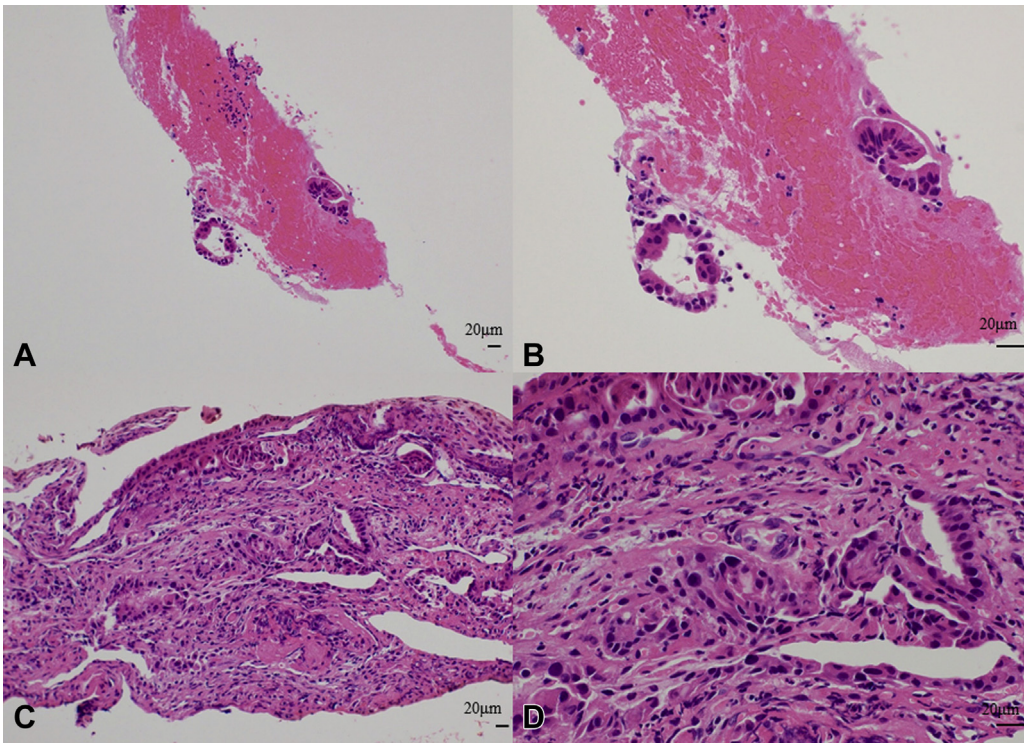

Figure 5. Histopathologic findings in biopsy samples. In the fluoroscopy-guided bile duct biopsy (**A,** H&E, orig. mag. ×200; **B,** H&E, orig. mag. ×400), the biopsy sample size was insufficient, and diagnosis was therefore not possible. In the peroral cholangioscopy-guided biopsy (**C,** H&E, orig. mag. ×200; **D,** H&E, orig. mag. ×400), a sample of sufficient size was collected. The biopsy samples contained atypical cells with hyperchromatic nuclei and eosinophilic cytoplasm. Similarly to probe-based confocal laser endomicroscopy findings, these formed a ductal structure with irregular margins. The nuclei showed marked size variation, irregular morphology, and irregular arrangement, indicating adenocarcinoma.

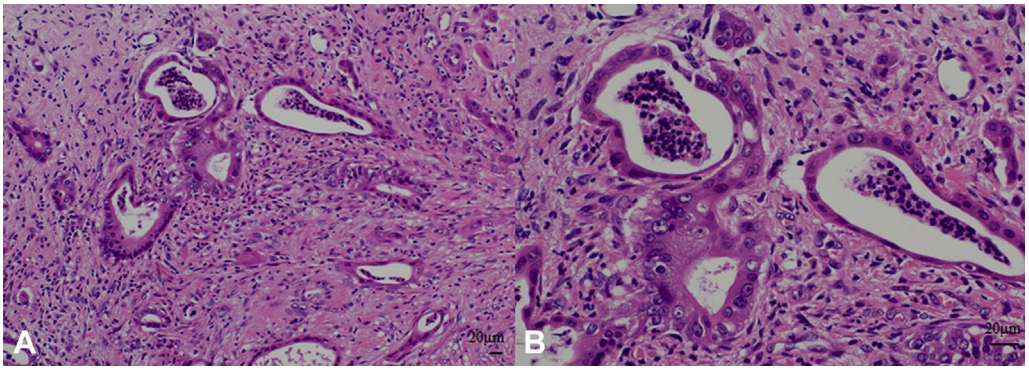

Figure 6. Histopathologic findings from surgical samples. **A,** H&E, orig. mag. ×200. **B,** H&E, orig. mag. ×400. The findings were similar to those from biopsy samples taken at peroral cholangioscopy. Irregular invasive proliferation by atypical bile ducts with eosinophilic cytoplasm was found, and the final diagnosis was pancreatic cancer.

Our experience with using POCS-guided pCLE to diagnose cancer in a patient with surgically altered anatomy may improve the efficacy of diagnosis in such patients with surgically altered anatomy.

DISCLOSURE

All authors disclosed no financial relationships relevant to this publication.

Abbreviations: pCLE, probe-based confocal laser endomicroscopy; POCS, peroral cholangioscopy.

REFERENCES

1. Nonaka K, Ohata K, Nakai Y. Probe-based confocal laser endomicroscopy of the duodenal mucosa with fluorescein dispersion. Dig Endosc 2014;26:604.
2. Nonaka K, Ohata K, Ichihara S, et al. Development of a new classification for in vivo diagnosis of duodenal epithelial tumors with confocal laser endomicroscopy: a pilot study. Dig Endosc 2016;28:186-93.

3. Meining A, Shah RJ, Slivka A, et al. Classification of probe-based confocal laser endomicroscopy findings in pancreaticobiliary strictures. Endoscopy 2012;44:251-7.
4. Meining A, Chen YK, Pleskow D, et al. Direct visualization of indeterminate pancreaticobiliary strictures with probe-based confocal laser endomicroscopy: a multicenter experience. Gastrointest Endosc 2011;74:961-8.
5. Tanisaka Y, Ryozawa S, Mizuide M, et al. Analysis of the factors involved in procedural failure: endoscopic retrograde cholangiopancreatography using a short-type single-balloon enteroscope for patients with surgically altered gastrointestinal anatomy. Dig Endosc 2019;31:682-9.
6. Navaneethan U, Hasan MK, Kommaraju K, et al. Digital, single-operator cholangiopancreatoscopy in the diagnosis and management of pancreatobiliary disorders: a multicenter clinical experience (with video). Gastrointest Endosc 2016;84:649-55.
7. Slivka A, Gan I, Jamidar P, et al. Validation of the diagnostic accuracy of probe-based confocal laser endomicroscopy for the characterization of indeterminate biliary strictures: results of a prospective multicenter international study. Gastrointest Endosc 2015;81:282-90.

Department of Gastroenterology, Saitama Medical University International Medical Center (1), Department of Pathology, Dokkyo Medical University, Saitama Medical Center (2); Saitama, Japan.

https://doi.org/10.1016/j.vgie.2019.11.011