

CASE REPORT

Normal bile duct findings using peroral cholangioscopy-guided probe-based confocal laser endomicroscopy (with video)

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Key words

capillary network just beneath the bile duct epithelium, Miami Classification, Normal bile duct, POCS-guided pCLE, reticular network of thin dark branching bands.

Accepted for publication 3 September 2019

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Declaration of conflict of interest: None.

Abstract

We encountered a case of wall thickening of the bile duct in a 69-year-old man. endoscopic retrograde cholangiopancreatography (ERCP) was performed for detailed examination. When an area considered to be the healthy bile duct was examined by peroral cholangioscopes (POCS) (SPYGlass DS), the vascular network was observed. POCS-guided, probe-based confocal laser endomicroscopy (pCLE; CholangioFlex, Cellvizio; Mauna Kea Technologies, Paris, France), performed using the fluorescein-dripping method on this area, showed a reticular network of thin dark branching bands, which were presumed to be a collagen bundle or lymphatic vessels according to the Miami Classification. However, 8 µm-diameter objects thought to be red blood cells were observed inside the bands, which were considered to correspond to the vascular network observed on POCS. A biopsy specimen of this site was taken. The histological examination demonstrated capillaries just beneath the bile duct epithelium. Thus, the histology also suggested the presence of the vascular network. In this study, we obtained findings that cannot be explained in terms of the Miami Classification, which we describe here with a video.

Introduction

The clinical diagnosis of biliary disease is based on a complex multimodality approach using computed tomography (CT), magnetic resonance imaging (MRI), endoscopic ultrasound (EUS), and endoscopic retrograde cholangiopancreatography (ERCP); however, these modalities are not definitive enough to obviate the need for histological confirmation. Probe-based confocal laser endomicroscopy (pCLE; CholangioFlex, Cellvizio; Mauna Kea Technologies, Paris, France) has been cited in the recent American Society for Gastrointestinal Endoscopy guidelines on the management of biliary neoplasia as a useful alternative to the existing diagnostic work-up.¹ Real-time microscopic images of the bile duct tissue are generated using a dedicated confocal miniprobe that enables *in vivo* histological assessment on the spot, known as “virtual biopsy.” Miami Classification is known as the criterion for differentiating a healthy bile duct from malignant stricture.² Using this criterion, the healthy bile duct is defined as follows: (i) reticular network of thin, dark, branching bands; (ii) light gray background; and (iii) vessels. On the other hand, malignant stricture is defined as follows: (i) thick white bands, (ii) thick dark bands, (iii) epithelium, and (iv) dark clumps. In a multicenter registry on 102 patients aimed at evaluating the performance of this technique to differentiate normal from malignant bile ducts using the Miami Classification, the investigators were asked to predict neoplasia in

an offline review of the pCLE videos acquired during the ERCPs.³ The sensitivity, specificity, and overall accuracy were 98, 67, and 81%, respectively, for pCLE, compared with 45, 100, and 75% for index pathology. In that study, accuracy for the combination of ERCP and pCLE using the Miami Classification was significantly higher than that with ERCP and tissue acquisition. Therefore, pCLE has the potential to overcome some of the inherent limitations of the tissue sampling techniques in establishing a pathological confirmation of the stricture and offers the ability to objectify patient management decision-making. However, in that study, using the Miami Classification, a confocal miniprobe was inserted through a catheter or cholangioscope and advanced either until its tip was visible during fluoroscopy or under direct cholangioscopic visualization, and it was positioned in direct contact with the mucosa at the site of interest. The pCLE finding was not observed directly by cholangioscopy in all cases, and the biopsy was not performed under direct visualization; hence, it is doubtful whether the pCLE findings obtained accurately matched the biopsy tissue.

More recently, digital single-operator peroral cholangioscopes (POCS), (SPY-DS, SpyGlass DS; Boston Scientific Corp., Hidaka, Saitama, Japan) are available. The SPY-DS provides favorable visualization owing to a digital field of view of 120° and newly added injection and suction functions. Moreover, POCS-guided pCLE is

useful because we can carry out pCLE under the direct view of POCS. pCLE of the region of interest under POCS guidance and directed biopsy are required to ensure that pCLE findings can be accurately matched up with biopsy tissue.

In this study, we performed POCS-guided pCLE and direct biopsy of the healthy bile duct and used the Miami Classification for diagnosis. However, we obtained findings that cannot be explained in terms of the Miami Classification, which we describe here with a video.

Case report

We encountered a case of wall thickening of the bile duct in a 69-year-old man. ERCP was performed for detailed examination (Video S1, Supporting information). The cholangiography did not show any bile duct abnormalities (Fig. 1a). When an area considered to be the healthy bile duct was examined by POCS (SPYGlass DS), a vascular network was observed (Fig. 1b). POCS-guided pCLE performed by the fluorescein-dripping method^{4,5} on this area showed a reticular network of thin dark branching bands, which were presumed to be a collagen bundle or lymphatic vessels according to the Miami Classification (Fig. 1c,d). However, 8 μm -diameter objects thought to be red blood cells were observed inside the bands (Fig. 1d), which were considered to correspond to the vascular network observed on POCS. A biopsy specimen of this site was taken. The histological examination demonstrated capillaries just beneath the bile duct

epithelium, which were further confirmed by the CD34-positive and D2-40-negative immunohistochemistry (Fig. 1e–h). Thus, the histology also suggested the presence of the vascular network. The pCLE image seemed to reflect the histological findings. We referred the patient to his previous doctor for follow-up. We asked him or her to contact us if any change occurred. Although about 1 year has passed, there are no changes in this patient so far.

Discussion

In previous studies,^{2,6,7} the authors presumed that the dark branching bands corresponded to lymphatics or thin collagen bundles. In this case, we confirmed that the vascular network observed using POCS corresponded to dark branching bands observed using pCLE. Moreover, we confirmed the presence of 8 μm -diameter objects inside the bands, presumed to be red blood cells. Because we obtained the biopsy specimen under direct view of POCS, we believe that the vascular network observed under POCS, the dark branching bands seen under pCLE, and the biopsy specimen are roughly the same. However, we cannot completely rule out the possibility that lymphatic or collagen fiber may present as such under pCLE. We should conduct further studies to prove these findings.

In summary, the reticular network of thin, dark, branching bands according to the Miami Classification may have actually represented the capillary network just beneath the bile duct epithelium, which needs to be confirmed by further studies.

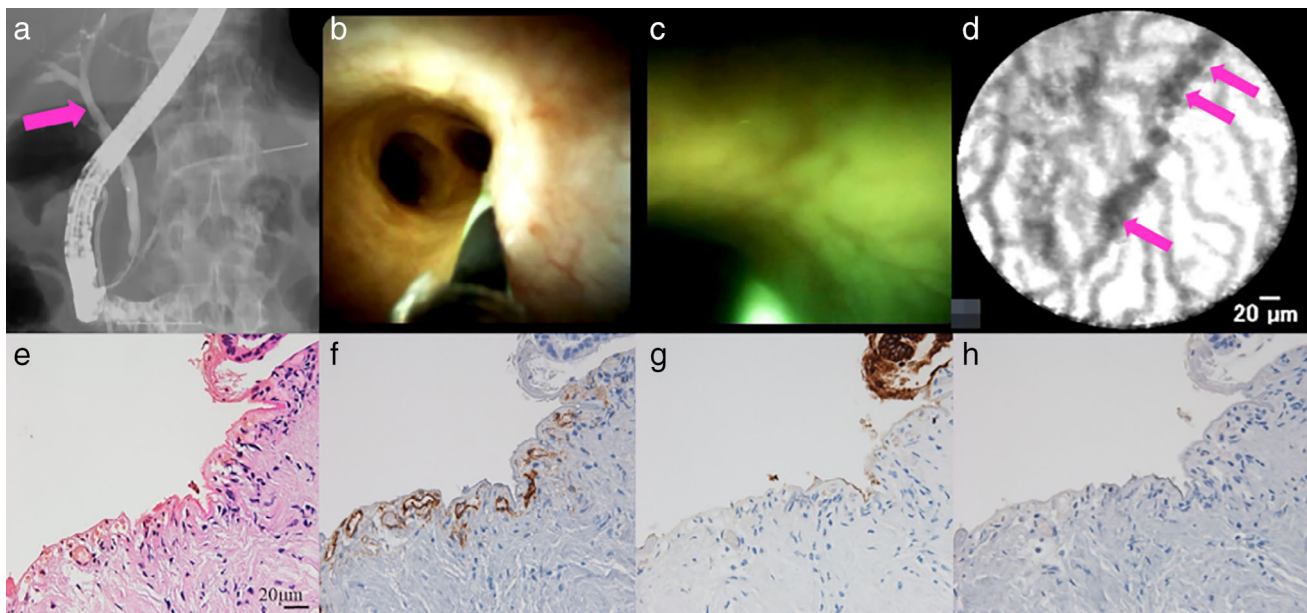


Figure 1 (a) The cholangiography did not show any bile duct abnormalities. (b) When an area considered to be the healthy bile duct ((a) pink allow) was examined by peroral cholangioscopy (POCS), a vascular network was observed. (c,d): POCS-guided, probe-based confocal laser endomicroscopy (pCLE; CholangioFlex, Cellvizio; Mauna Kea Technologies, Paris, France), performed using the fluorescein-dripping method on this area, showed a reticular network of thin dark branching bands; 8 μm -diameter objects thought to be red blood cells were observed inside the bands (pink allow). (e) The histology of the biopsy demonstrated capillaries just beneath the bile duct epithelium, which was detached artificially (HE, orig. Mag. $\times 400$). (f) Immunostaining of CD34, which was positive for the capillaries beneath the epithelium (orig. Mag. $\times 400$). (g) Immunostaining of CK7, which was positive for the artificially detached bile duct epithelium (orig. Mag. $\times 400$). (h) Immunostaining of D2-40, indicating the absence of lymphatic channels beneath the epithelium (orig. Mag. $\times 400$).

References

- 1 American Society for Gastrointestinal Endoscopy (ASGE) Standards of Practice Committee, Anderson MA, Appalaneni V, Ben-Menachem T *et al.* The role of endoscopy in the evaluation and treatment of patients with biliary neoplasia. *Gastrointest. Endosc.* 2013; **77**: 167–74.
- 2 Meining A, Shah RJ, Slivka A *et al.* Classification of probe-based confocal laser endomicroscopy findings in pancreaticobiliary strictures. *Endoscopy.* 2012; **44**: 251–7.
- 3 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.
- 4 Nonaka K, Ohata K, Nakai Y. Probe-based confocal laser endomicroscopy of the duodenal mucosa with fluorescein dispersion. *Dig. Endosc.* 2014; **26**: 604.
- 5 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.
- 6 Caillol F, Bories E, Autret A *et al.* Evaluation of pCLE in the bile duct: final results of EMID study : pCLE: impact in the management of bile duct strictures. *Surg. Endosc.* 2015; **29**: 2661–8.
- 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.

Supporting information

Additional supporting information may be found in the online version of this article at the publisher's website:

Video S1. The cholangiography did not show any bile duct abnormalities. When an area considered to be the healthy bile duct was examined by peroral cholangioscopes (POCS) (SPYGlass DS), a vascular network was observed. POCS-guided pCLE, performed using the fluorescein-dripping method on this area, showed a reticular network of thin dark branching bands, which were presumed to be a collagen bundle or lymphatic vessels according to the Miami Classification. However, 8 μm -diameter objects thought to be red blood cells were observed inside the bands, which were considered to correspond to the vascular network observed on POCS. A biopsy specimen of this site was taken.