

A combination of biopsy using eyeMAX and ERCP for the definitive diagnosis of intraductal papillary mucinous neoplasm: A case report

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Abstract. As a well-established precursor lesion of pancreatic cancer, intraductal papillary mucinous neoplasm (IPMN) of the pancreas remains characterized by notable challenges with regard to diagnosis and treatment. Owing to its heterogeneous biological behavior, which can range from benign lesions to invasive carcinomas, IPMN represents a marked clinical challenge in management. Biopsy in addition to endoscopic retrograde cholangiopancreatography (ERCP) using eyeMAX can aid in the development of an individualized treatment plan. The present report outlines the case of a patient with suspected IPMN who was admitted to Shandong Provincial Hospital Affiliated to Shandong First Medical University (Jinan, China). Endoscopic ultrasound examination revealed a dilated main pancreatic duct (MPD). The duodenal papilla showed signs of a fish mouth covered with mucus through observation by a duodenoscope. The patient refused the surgical treatment due to concerns regarding the risks of surgery. Subsequently, aided by ERCP using eyeMAX, the villus-like and papillary protrusions were visualized intuitively in the MPD wall of the pancreatic head segment. A total of four pieces of tissue were taken from the pancreatic duct for biopsy, with pathology revealing low-grade dysplasia. Furthermore, direct observation revealed that the wall of the body-tail portion of the MPD was smooth. Given that the pathology revealed a low malignant transformation tendency, it was decided that a follow-up strategy would be conducted for the patient. The most recent follow-up occurred in July 2026. The patient was generally in good condition without jaundice, pancreatitis or abdominal

pain. Therefore, biopsies based on ERCP using eyeMAX may be helpful in developing individualized treatment plans for patients with IPMNs in the future.

Introduction

Intraductal papillary mucinous neoplasm (IPMN) of the pancreas is among the most well-established precursors of pancreatic cancer (1-3). A meta-analysis included 51 studies mainly from Japan, the USA and France revealed that the prevalence rates of cancer in IPMN arising in main duct and mixed type IPMN can reach 39% (4). IPMN can be divided into main duct IPMN, branch duct type and mixed type (5) based on the location of the lesion site. The transformation of IPMNs in pancreatic cancer is progressive and occurs through low-grade dysplasia, high-grade dysplasia and ultimately invasive cancer. Jaundice, enhancing mural nodules measuring >5 mm, main pancreatic duct (MPD) dilation >10 mm and the cytological conformation of high-grade dysplasia represent high-risk stigmata (HRS) of malignant transformation (6). IPMN diagnosis is primarily based on noninvasive and invasive imaging techniques. Modalities, including MRI, CT and endoscopic ultrasound (EUS) are extensively applied for evaluating disease activity and tracking disease progression (7,8). In recent years (9), endoscopic retrograde cholangiopancreatography (ERCP) has been recognized as one of the principal approaches used in IPMN diagnosis (10), especially with the development of eyeMAX. The eyeMAX (Micro-Tech; Nanwei Medical Technology Co., Ltd.) is a novel disposable biliary imaging system. It can pass the working channel of endoscopes to reach bile duct and pancreatic duct. Pancreatic duct diseases, such as pancreatobiliary stricture, pancreatic stone are indications for eyeMAX (11). Given the malignant potential of IPMNs (9), the main treatment method is surgical excision. Despite this, a proportion of these patients who fulfill surgical criteria may be considered ineligible for surgery owing to surgical contraindications or considerations associated with high surgical risks, such as pancreatic fistula and postoperative bleeding. Therefore, defining the pathology of IPMNs before determining treatment could help doctors develop precise and personalized treatments; however, this remains a clinical challenge. In the present study, visualization

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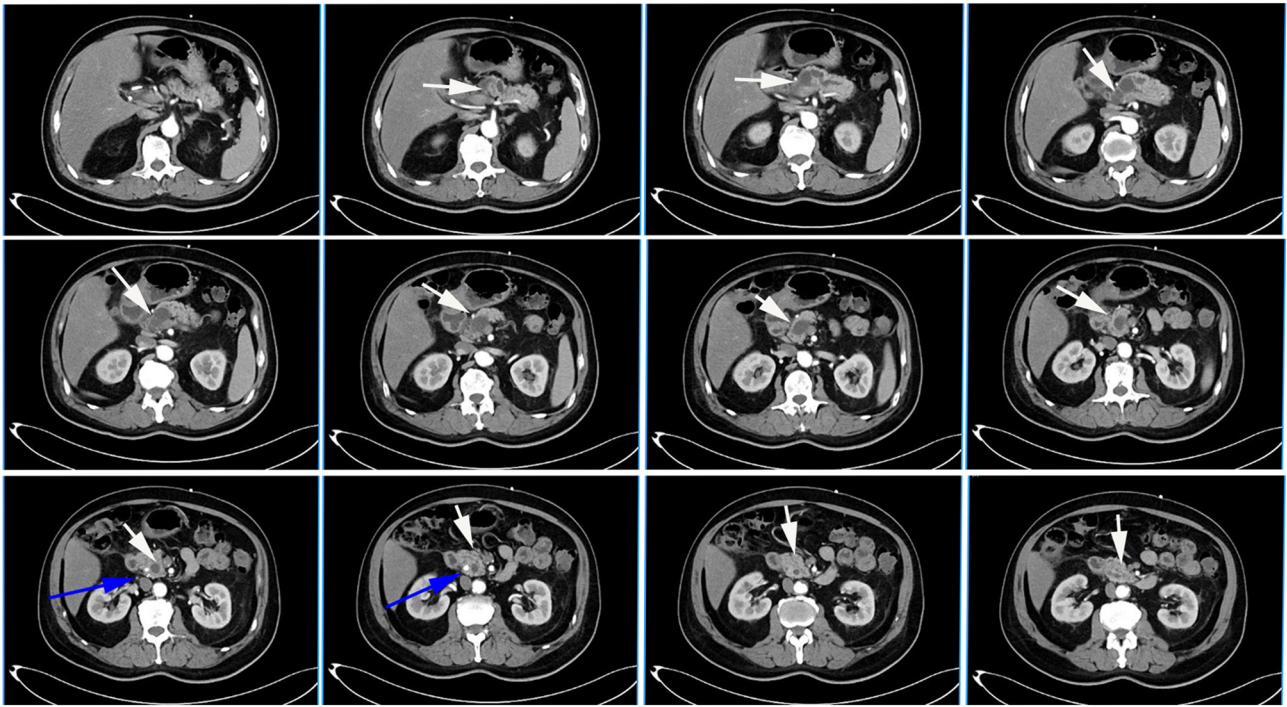


Figure 1. Signs of the lesions on CT. CT showing dilatation of the main pancreatic duct and branch pancreatic duct with cystic changes. The white arrows indicate the cyst of the intraductal papillary mucinous neoplasm and the dilated pancreatic duct. The blue arrows indicate stones in the common bile duct.

of the lesion was possible and biopsy was performed with the aid of eyeMAX during ERCP, which helped achieve more accurate treatment for the present patient.

Case report

A male patient aged 71 years was admitted to Shandong Provincial Hospital Affiliated to Shandong First Medical University (Jinan, China) in August 2025 with symptomatic abdominal distress and abdominal distension. An initial CT scan (Fig. 1) and MRI (Fig. 2) exhibited dilatation of the MPD and branch pancreatic duct (BPD) with small cystic changes, meaning IPMNs could not be completely excluded. In addition, the CT scan revealed the presence of gallstones in the common bile duct (CBD). The CA19-9 (normal reference range, 0-37 IU/ml) concentration was >1,000 IU/ml and CEA was 4.0 ng/ml (normal reference range, 0-5 ng/ml). CA19-9 was measured by electrochemiluminescence immunoassay. Sample was incubated with biotin labeled anti-CA19-9 specific monoclonal antibody and ruthenium (Ru)^a-labeled anti-CA19-9 specific monoclonal antibody to form an antigen-antibody sandwich complex. Streptavidin-coated magnetic beads were added for incubation, and the complex bound to the magnetic beads via biotin-streptavidin interaction. The reaction mixture was aspirated into the measuring cell, and magnetic beads were captured onto the electrode surface by electromagnet force. Unbound substances were removed using ProCell II M. A defined voltage was applied to the electrode to trigger chemiluminescence of the complex, and luminescence intensity was measured by a photomultiplier tube. The test result was automatically calculated by the instrument using a two-point calibrated calibration curve and the master curve obtained via cobas link. The patient was therefore diagnosed with a

pancreatic mass and suspected IPMN. An EUS (Fig. 3) was subsequently performed, revealing that the cystic lesion and MPD of the patient was dilated (Fig. 3A-F), with the widest point being 11.5 mm (Fig. 3H). There was no obvious dilation of CBD (Fig. 3G).

After the preoperative surgical conversation, the patient eventually refused surgery due to concerns regarding the potential risks. In accordance with a multidisciplinary team discussion, it was decided that an attempt would be made to obtain the pathology of the IPMN and subsequently develop a further treatment plan. ERCP was subsequently adopted in August 2025 to remove gallstones in the CBD and to further clarify the lesions of the pancreas (Fig. 4). The duodenal papilla exhibited signs of a fish mouth (the opening of duodenal papilla was significantly enlarged and the shape was round and blunt, similar to the 'fish mouth') covered with mucus through observation using a duodenoscope (Fig. 4A). On the basis of the ERCP using eyeMAX, villus-like and papillary protrusions were visualized intuitively in the MPD wall of the pancreatic head segment (Fig. 4B) and a total of four pieces of tissue were taken for biopsy (Fig. 4C). The wall of the body-tail portion of the MPD was smooth (Fig. 4D-F). A HistoCore SPECTRA H&E Staining System S2 (filing no. 20170724; Leica Biosystems) with fully automatic programming was used for H&E staining. This system worked based on the HistoCore SPECTRA ST Stainer. Furnished with a built-in barcode system, it enables accurately tracking of different slides. Through an integrated dual translational robotic arm, it can store and parallelly execute H&E staining procedures. An integrated oven was incorporated in the device, which simplifies the workflow by removing the need of the external heating unit. The stainer can be directly integrated with Leica HistoCore

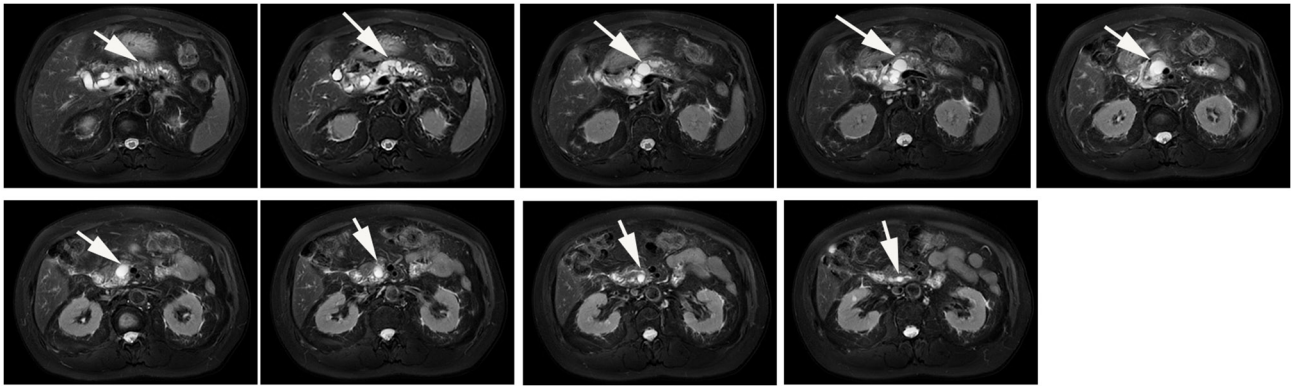


Figure 2. Signs of the lesions on MRI. MRI showing dilatation of the main pancreatic duct and branch pancreatic duct with cystic changes. The arrows indicate the cystic structure of the intraductal papillary mucinous neoplasm and the dilated pancreatic duct.

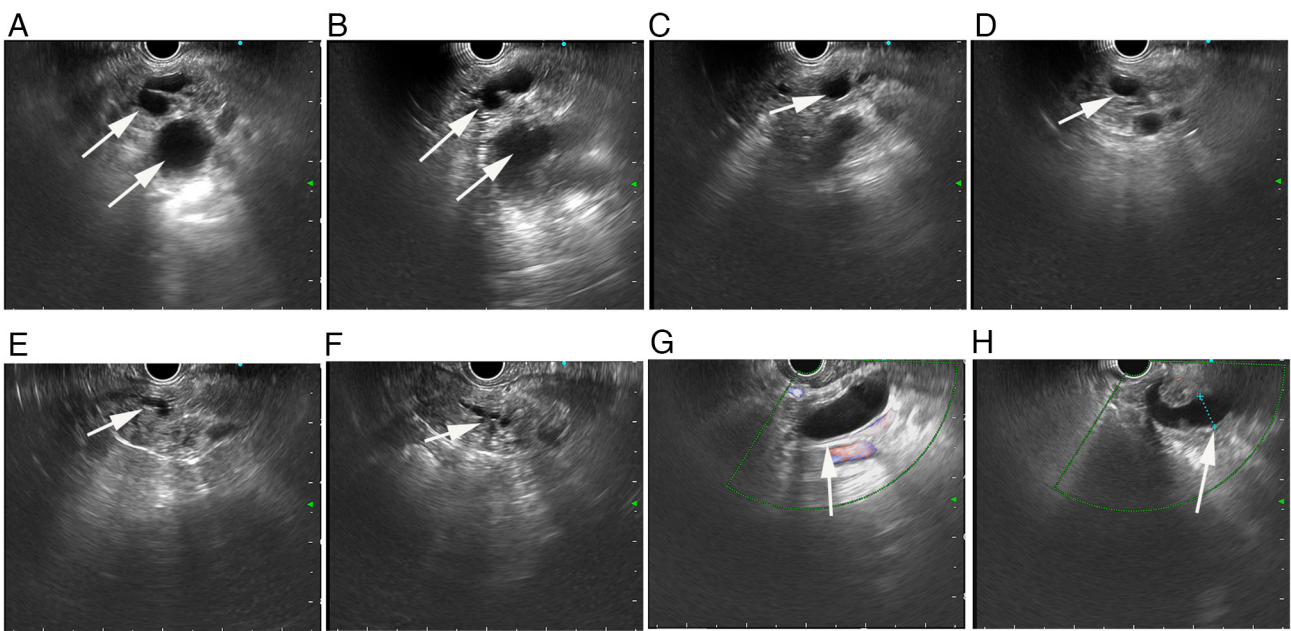


Figure 3. Signs of the lesions on endoscopic ultrasound. (A-F) The white arrows indicate cystic lesions and dilated pancreatic duct examined by EUS. No mural nodule was detected in the cyst. (A) The cystic lesions and dilated pancreatic duct at pancreatic head segment. (B) The cystic lesions and dilated pancreatic duct at pancreatic neck segment. (C) Dilated pancreatic duct at pancreatic body segment. (D) Dilated pancreatic duct at pancreatic body segment. (E) Pancreatic duct at pancreatic tail segment. (F) Pancreatic duct at pancreatic tail segment. (G) The common bile duct without obvious dilation. (H) The widest point of main pancreatic duct was 11.5 mm, as indicated by the blue dashed line.

SPECTRA CV coverslip (12). Finally, the biopsy sections were observed through OLYMPUS microscope (BX53) and images were captured. Furthermore, the pathology revealed low-grade dysplasia (Fig. 5). No adverse events regarding the patient occurred following ERCP or biopsy. Given that the pathology revealed a low malignant transformation tendency, it was decided that a follow-up strategy, including monitoring abdominal imaging and CA19-9 would be conducted for the patient. The patient was discharged at the end of August, 2025 and has remained in good condition. The most recent follow-up occurred in July 2026. The patient was reported to be in a good general condition without jaundice, pancreatitis or abdominal pain. The CA19-9 concentration of the patient was reported to be 27.284 IU/ml and CEA was 2.751 ng/ml at the latest follow-up (Fig. 6A). The patient underwent an enhanced MRI examination again in July 2026. Compared

with the previous scan, the MPD was shown to be slightly dilated. No notably enhanced mural nodules or other malignant features were detected (Fig. 6B and C).

Discussion

IPMNs are a mucin-producing subtype of the pancreatic cyst lesions arising from the pancreatic duct system (6) and are difficult for diagnosis and treatment. It has been estimated that up to 49.1% of individuals who have undergone cross-sectional imaging have incidentally detected pancreatic cystic lesions (13). CT and MRI serve as the main imaging modalities for the diagnosis of IPMNs which have typical and characteristic CT and MRI features (14). CT provides excellent spatial resolution and is especially efficient in evaluating pancreatic ductal adenocarcinoma (PDAC), vascular invasion

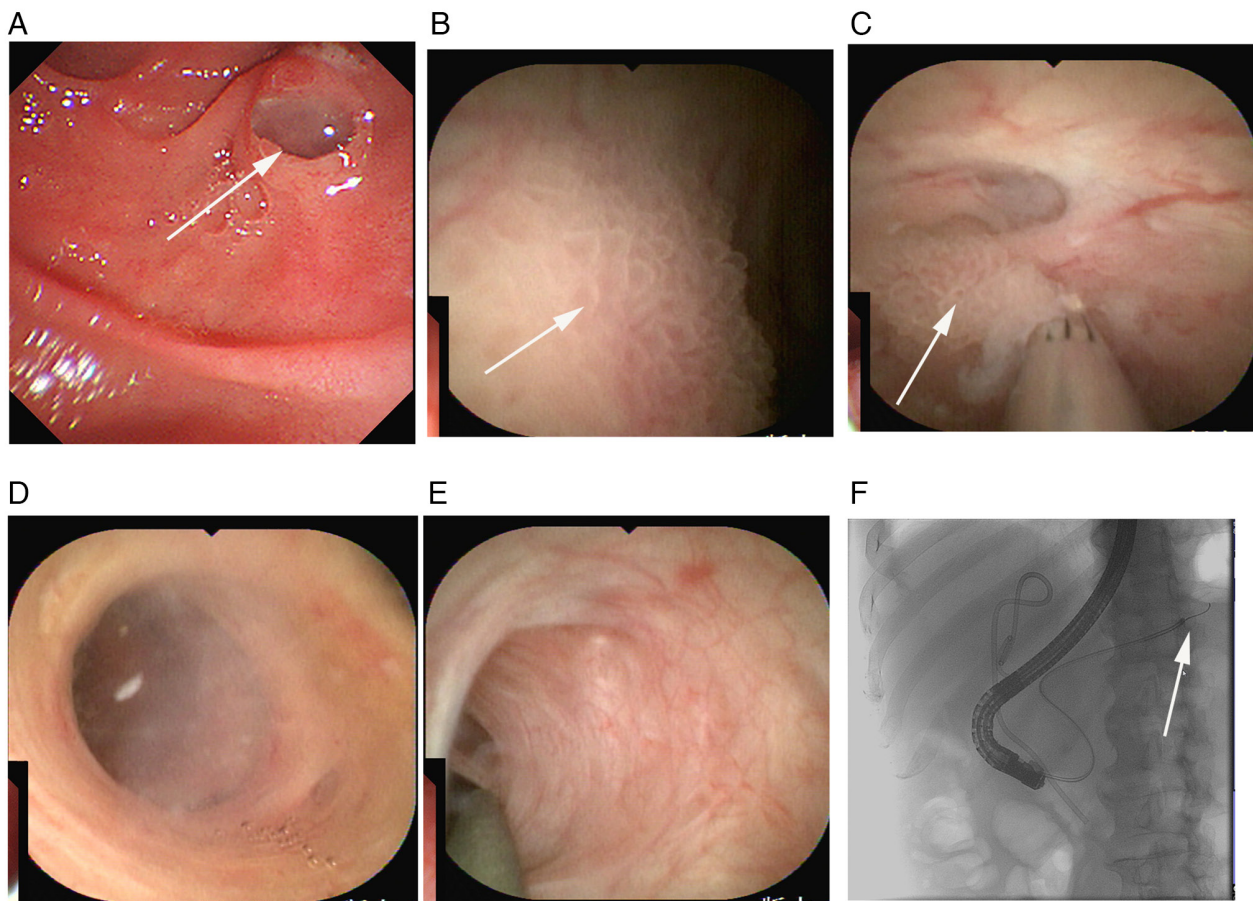


Figure 4. Endoscopic retrograde cholangiopancreatography imaging using eyeMax. (A) Duodenal papilla showing a fish mouth sign covered with mucus through the observation of duodenoscopy, as shown by the white arrow. (B) Villus-like and papillary protrusions were visualized intuitively in the main pancreatic duct wall of the pancreatic head segment, as shown by white arrows. (C) The sample was obtained by eyeMAX Bite. (D) The wall of the body-tail portion of main pancreatic duct. (E) The wall of the body-tail portion of main pancreatic duct was smooth. (F) The X-ray image of eyeMAX in MPD. The white arrow indicates that the guidewire in eyeMAX reached the pancreatic duct at the tail segment.

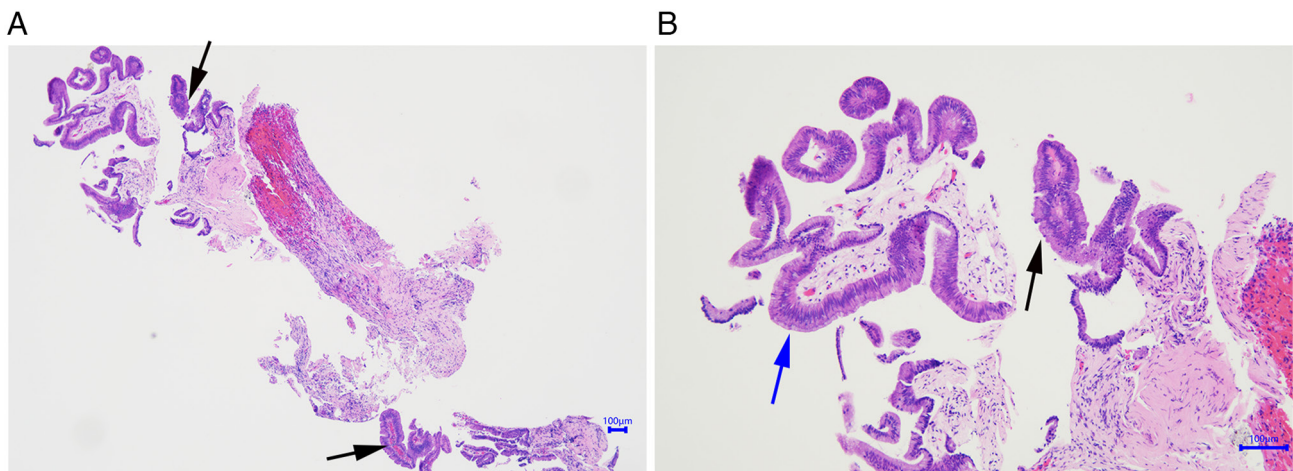


Figure 5. Pathology of the lesion. Pathological analysis revealed that the lesion presented with low-grade dysplasia. (A) Biopsy tissue of the pancreatic mass. A small amount of hyperplastic fibrous tissue with hemorrhage can be seen in the central area. Epithelial components can be seen on both sides and papillary structures can be observed in some areas, as shown by the black arrows (H&E staining; magnification, x40). (B) The epithelial component was a single-layer mucus columnar epithelium. The nucleus exhibited low-grade dysplasia and the cytoplasm contained a mucus component, as shown by the blue arrow. The black arrow shows the papillary structure composed of the fibrous vascular axis and the epithelial component (H&E staining; magnification: x100).

and metastatic diseases. On the contrary, MR provides superior soft tissue contrast and ductal delineation, allowing

detailed assessment of subtle stenosis, cystic lesions, and intraductal abnormalities (15). Notably, CT serves a dominant

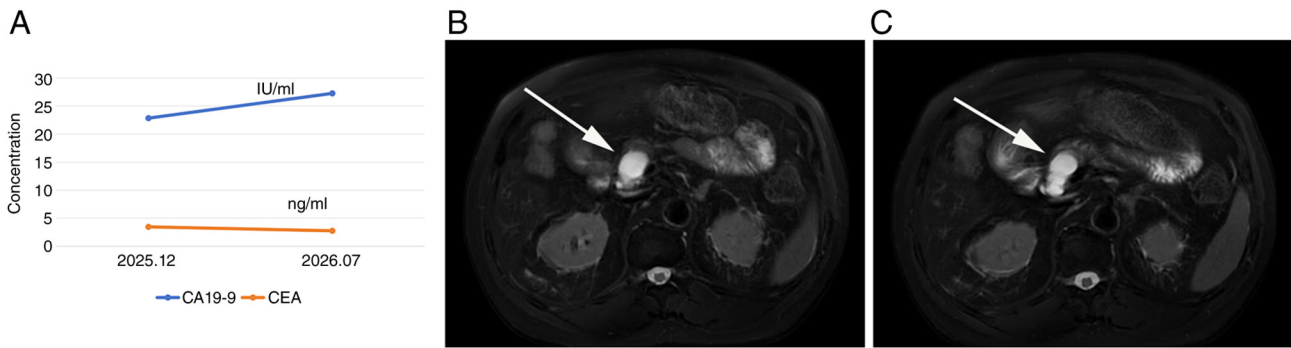


Figure 6. Follow-up examination results. Dynamic changes in CA19-9 and CEA levels and MRI reexamination results. (A) The CA19-9 and CEA levels were within the normal range at the two follow-up examinations after endoscopic retrograde cholangiopancreatography. (B) No notably enhanced mural nodules or other malignant features were detected. (C) Compared with the previous scan, the main pancreatic duct (shown by the white arrows) was slightly dilated.

role in the evaluation of IPMNs; however, delineating the connection between the cystic lesion and duct system is difficult partly because the intravenous contrast cannot opacify the duct lumen (16). MRI/MRCP is the preferred initial method because it has advantages in distinguishing benign from malignant IPMNs and similarly, MRI/MRCP is the preferred choice for long-term follow-up (17). In accordance with the European evidence-based Guidelines, EUS is recommended as an auxiliary imaging modality when clinical or radiological findings cannot exclude malignant transformation of IPMNs (18). EUS-fine-needle aspiration should be performed when conventional radiological and EUS features fail to yield a confirmed diagnosis (19); however, its accuracy is low to a certain extent. Peroral pancreatoscopy based on ERCP facilitates the diagnosis of IPMN, especially with the development of eyeMAX in recent years (20). By benefitting from image processing algorithms and eyeMAX, eyeMAX bite, not only can high-resolution images be obtained, but also biopsy can be performed (21,22). In addition, compared with previous pancreatoscopy methodologies, eyeMAX allows more detailed observation of blood vessels and glandular ducts and provides more representative images for further analysis. In patients with suspected IPMN, who exhibit a dilated MPD but no obvious mural nodule detected by EUS, the eyeMAX clearly displays the microstructure of the lesion and acquires sufficient pathological tissue. These factors also help to differentiate IPMN from other pancreatic cystic lesions such as mucinous cystic neoplasms and serous cystadenomas. In addition, eyeMAX more easily reveals lesions of the distal pancreatic duct and has more economic advantages, which is important for the majority of patients (21,23). In general, the combination of CT, MRI, EUS and ERCP using eyeMAX resulted in a more accurate diagnosis of IPMN and helped to determine a more precise treatment for the present patient. In addition, biopsy, improved cell block processing, and marker identification were helpful for the diagnosis and selection of individualized treatment (24-26).

The biological behavior of IPMNs ranges from benign to invasive malignancy. Despite clinicians making their best efforts to evaluate the lesions as extensively as possible, a portion of patients with benign cysts may receive unnecessary surgical resection, whereas lesions that are deemed appropriate for surveillance can eventually progress to malignancy.

In accordance with Kyoto guidelines for managing pancreatic IPMN, an MPD diameter ≥ 10 mm constitutes one of the HRSs indicating elevated malignant potential (7). In addition, a previous retrospective cohort study suggested that an MPD diameter of 7.2 mm or greater had the highest diagnostic accuracy and was an independent predictor of malignancy in patients with MD or mixed IPMNs (27). This study further argued that a lower MPD diameter threshold should be recognized as a criterion for surgical management (27). However, surgical resection is associated with notable risks of morbidity and mortality (28).

In the present case, before the originally planned surgery, the patient underwent CT, MRI and EUS examinations. Thus, surgery was recommended first. As the patient refused resection of the lesion and at the same time, a stone in the CBD was found, ERCP was performed and the eyeMAX was also used. Unlike CT, MRI, EUS and ERCP, lesions can only be evaluated through indirect imaging. Through eyeMAX, images of the lesion were directly obtained and targeted biopsy was performed under direct visualization. Pathology of the lesion revealed low-grade dysplasia, and eventually, the patient accepted a follow-up plan and was in good condition for ~ 1 year after the biopsy.

Despite the biopsy result being reassuring in the present patient, a limited biopsy from the pancreatic duct cannot necessarily exclude high-grade dysplasia or invasive carcinoma elsewhere in the lesion, particularly in the context of main pancreatic duct dilatation >10 mm. Therefore, the pathology acquired through biopsy may not be able to represent the entirety of the lesion. In general, it is necessary for clinicians to perform multiple or regular biopsies; however, the diagnosis of IPMN in the present patient was based on biopsy, imaging examination (including CT and MRI) and endoscopy (including EUS and ERCP) and given that complete pathological specimens of the lesion were unobtainable, other cystic diseases of the pancreas could not be completely excluded. Notably, in the present case, the elevated CA19-9 and the pancreatic duct width greater than 10 mm were considered HRSs of IPMN. However, firstly, the present patient could not bear the risk of surgery and secondly, the pathology revealed low-grade dysplasia and no obviously tortuous or dilated blood vessels were detected by eyeMAX. Thus, a follow-up strategy was adopted for the present patient. Importantly, the decision

to pursue follow-up should not be presented as a generally preferable option for patients with low-grade dysplasia. In the present case, it was chosen as an individualized approach after multidisciplinary discussion because the patient declined surgical resection. CA19-9 is an important biomarker for malignant pancreatic tumors (29); however during biliary tract inflammation, CA19-9 may be elevated and usually declines after infection is controlled. In the present patient, the serum CA19-9 concentration was markedly high before stone removal from the CBD and returned to the normal level after the operation. Thus, in the present case, the increase in CA19-9 was considered to be associated with inflammation and obstruction of the CBD secondary to stones.

Overall, the findings from the present case highlight the importance of biopsy acquired through eyeMAX based on ERCP without causing high risks, which exhibited an important diagnostic value for guiding the formulation of a treatment plan for the present patient. Despite there being many sampling limitations, more patients with pancreatic diseases may benefit from the development of eyeMAX on the basis of CT, MR, EUS and ERCP. In the future, the guidelines may be more optimized and meticulous with the development of technology to obtain biopsies of IPMNs.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

WW and TL designed and conceptualized the present study. Data acquisition and curation were implemented by WW and JH. The initial draft was written by WW, with ZL and YY contributing to manuscript revision, reviewing and editing. All authors were responsible for all aspects of the research in order to ensure the accuracy and integrity of the work. WW and YY confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

The present patient provided written informed consent to publish the present case report and the associated images. The

patient was notified that all identifiable personal data would be deleted to protect their privacy.

Competing interests

The authors declare that they have no competing interests.

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