A 53-year-old female patient visited our hospital for dyspepsia of 3-month duration. She had no specific medical or surgical history. Her vital signs at admission were blood pressure 110/70 mmHg, pulse rate 82/min, respiratory rate 20/min, and body temperature 36.3°C. Physical examination revealed no marked features. The laboratory data also showed no abnormalities, including tumor markers (CEA 1.0 ng/mL, CA 19–9 2.0 U/mL). Screening upper gastrointestinal endoscopy showed protruding major papilla and subsequent endoscopic biopsy of the major papilla revealed low-grade adenoma. A duodenoscopic image showed an enlarged major papilla with central umbilication and fine nodularity. EUS at the major ampulla revealed a 1.1 × 0.9 cm, slightly hypoechoic round ampullary mass confined to the submucosa without definite wall disruption or adjacent invasion (Fig. 1). Abdomen CT did not show an abnormally dilated pancreatic or biliary duct, ductal invasion, or enlarged lymph nodes.

Based on pathology and an imaging study, we planned endoscopic papillectomy for the removal of unexposed ampullary adenoma. Following submucosal injection of 1:10,000 epinephrine, snaring papillectomy was performed. However, complete resection of major papilla was unsuccessful. Following the first papillectomy, a remnant, whitish, round mass-like lesion was seen to protrude, and was difficult to differentiate from remnant tumor or a second combined

**Figure 1** (A) A duodenoscopic image shows an enlarged major papilla with central umbilication and fine nodularity. (B) Endoscopic ultrasonography at the major ampulla reveals a 1.1 × 0.9 cm, slightly hypoechoic round ampullary mass confined to the submucosa without definite wall disruption or adjacent invasion.
tumor. Therefore, a second resection was performed successfully in the same manner as the first one. An endoscopic image acquired immediately following the two-step papillectomy showed complete resection without complications. Resected tissues showed a papillary roof lesion and a whitish, round, mass-like lesion (Fig. 2). Insertion of a prophylactic pancreatic stent failed due to technical difficulties with selective pancreatic duct cannulation. Due to the risk of post-procedure pancreatitis, the number of attempts to cannulate the pancreatic duct was not permitted to exceed five. Post-ERCP pancreatitis was not occurred.

Microscopic findings of the resected specimens were as follows. The protruding lesion was composed of two lesions that differed in their histological characteristics: tubular adenoma and neuroendocrine tumor (NET). The tubular adenoma lesion exhibited round-to-oval enlarged glands with stratified epithelial cells. The neuroendocrine tumor showed cord-like arrangement of monotonous tumor cells. Immunohistochemistry showed that the tumor cells were positive for synaptophysin (Fig. 3).

Follow-up endoscopic biopsy of the papillectomy site performed one and three month later did not show remnant tumor except reepithelization (Fig. 4). No local recurrence or metastasis of NET or adenoma was detected during 20 months of follow-up.
NET of the ampulla of Vater, formerly known as carcinoid tumors, is extremely rare. It accounts for only 0.3–1% of all gastrointestinal NETs, and less than 2% of all periampullary cancers. The natural history of this disease entity has not been well established.

Well-differentiated (low and intermediate grade) NETs have been variously termed carcinoid tumour (typical and atypical), neuroendocrine tumor (grade 1 and 2), or neuroendocrine carcinoma (low and intermediate grade). The previously used term, carcinoids of the ampulla of Vater, comprises a broad spectrum of morphologically and biologically diverse tumors. In the latest World Health Organization (WHO) classification, published in 2010, it is recommended to distinguish among 1. neuroendocrine...
neoplasm, grade 1 (low grade), 2. neuroendocrine neoplasm, grade 2 (intermediate grade), and 3. neuroendocrine carcinoma, grade 3 (high grade). Clinically, NET can cause carcinoid syndrome, which presents as diarrhea or facial flushing, due to increased secretion of serotonin. However, carcinoid syndrome in ampullary NET is rare and the clinical and laboratory findings typical of carcinoid syndrome are frequently absent. Anatomically, ampullary NET develops at the conjugation of the pancreatic and biliary ducts. Jaundice is the predominant symptom (53%) at the time of admission to hospital, followed by pain (24.6%), acute pancreatitis (6.0%) and weight loss (3.7%). The case presented herein exhibited no specific symptoms due to the tumor, with the exception of mild dyspepsia.

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The diagnosis of ampullary NET is challenging till now. This tumour frequently originates from the deep mucosa or submucosa, so that cannot easily be detected in biopsy specimens. Most reports describe such lesions as a round or oval mass, with intact overlying duodenal mucosa, with negative biopsies. Also, early lymphatic metastasis is possible despite the small size of the lesions, and an accurate diagnosis is difficult. Accuracy rates of biopsy for the preoperative diagnosis of NET range from to 14 to 66%. Duodenoscopy in combination with ERCP is the diagnostic method of choice for deeper biopsies with the aim of identifying intrapapillary lesions. EUS, CT or MRI are used for staging and differential diagnosis, together with detection of invasion of the biliary or pancreatic duct and metastasis to lymph nodes or other organs.

The treatment of choice for NET is complete resection. Metastasis is rare, particularly in ampullary NETs. Therefore, complete resection is required as the primary therapy. In terms of prognosis, the 5-year survival rate of completely resected NET exceeds 95%. The classical partial pancreatoduodenectomy (Kausch–Whipple operation) or pylorus-preserving pancreatoduodenectomy (PPPD) are considered the treatments of choice for ampullary NETs >2.0 cm in diameter. The mortality and morbidity rates for the two approaches are less than 5% and 15%, respectively. Alternatively, in patients with multiple comorbidities or elderly individuals, conservative treatment or minimally invasive endoscopic papillectomy should be considered.

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Local excision may be an option for the treatment of ampullary NET if the tumor is small and there is no evidence of regional lymph node or distant metastasis. Compared to local surgical excision, endoscopic papillectomy may be less harmful to the patient and reduce the hospital stay duration, and complete resection is possible in selected patients. Similar to the management of an ampullary adenoma, endoscopic papillectomy may be a reasonable alternative to surgical resection. When endoscopic papillectomy is decided upon, the differentiation of NET, tumor size, and lymph node metastasis should be considered. Endoscopic papillectomy may be a good alternative in highly differentiated tumors that do not infiltrate the muscularis, tumors <2 cm in size, and with no distant metastasis. The prognosis is reported to be excellent, with an overall 5-year survival rate of 90%.

The case presented herein was initially diagnosed as an ampullary adenoma and subsequently confirmed to be combined NET by endoscopic papillectomy. Surgical resection was not performed due to successful complete endoscopic resection and imaging studies did not show lymph node or distant metastasis.

To the best of our knowledge, this is the first reported case of endoscopic papillectomy for ampullary NET accompanied by adenoma in the English-language literature. This case was diagnosed initially...
as an ampullary adenoma (low grade) by endoscopic biopsy during screening endoscopy. Following endoscopic papillectomy for removal of adenoma, the lesion was diagnosed as NET, grade 1 (<2 mitoses/10 high power field and Ki67 index<3%) accompanied by low-grade adenoma. Pathologically deep resection margin was not clear for the tumor; however, no evidence of local or distant metastasis was detected by repeated biopsies and radiologic examination during 20 months of follow-up.

In general, low-grade ampullary adenoma is a common indication for endoscopic papillectomy. Indeed, well-differentiated ampullary NET is also a good candidate for complete endoscopic resection in selected indications. The clinical or pathological correlation between NET and adenoma is unclear but completely resected by endoscopic papillectomy following diagnosis of adenoma on the surface of major papilla. Further clinical follow-up is needed to confirm the long term clinical outcome.

REFERENCES