Treatment of ampullary neuroendocrine tumor by endoscopic snare papillectomy

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Patient: Female, 45
Final Diagnosis: Neuroendocrine tumor
Symptoms: Abdominal pain
Medication: —
Clinical Procedure: —
Specialty: Gastroenterology and Hepatology

Objective: Unusual setting of medical care
Background: Neuroendocrine tumor of the ampulla of Vater is extremely rare and is generally a low-grade endocrine cell tumor. The merits of radical vs. local resection remain uncertain.

Case Report: A 45-year-old female patient presented with abdominal pain lasting for 2 months. Papilla that was tumor-like macroscopically was seen in the second part of the duodenum in endoscopic retrograde cholangiopancreatography. Biopsy was histologically confirmed as a low-grade neuroendocrine tumor. No lymphadenopathy or visceral metastasis was found on an abdominal CT scan, In-111 octreotide scan, and EUS. The ampulla was removed by endoscopic snare papillectomy. All margins of resection were negative for tumor.

Conclusions: Endoscopic snare papillectomy may be the first step in the management of neuroendocrine tumors of the ampulla of Vater in high-risk surgical candidates and selected patients such as those with a well differentiated, low-grade, small tumor without regional/ distant metastasis. However, it can also be used in younger patients who wish to avoid surgical resection.

Key words: neuroendocrine tumor • ampulla of Vater • endoscopic papillectomy • endoscopic retrograde cholangiopancreatography

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Background

Neuroendocrine tumors are generally recognized to be low-grade endocrine cell tumors derived from the endoderm. Although they may be seen at any site in the whole gastrointestinal system, the most commonly involved areas are the appendix, distal small intestine, rectum, and stomach. Neuroendocrine tumors of the ampulla of Vater are extremely rare [1]; therefore, the natural history of this disease entity has not been well established, but it has been postulated that the prognosis is generally good. The clinical and laboratory findings of carcinoid syndrome are absent in patients with a neuroendocrine tumor of the ampulla [1,2]. A small percentage of neuroendocrine tumors of the ampulla of Vater can show more aggressive behaviors, such as distant metastasis. Therefore, the standard treatment of this entity has been complete surgical resection. The ampulla of Vater is a complex structure, and is the conflu-ent portion of the common bile duct and the pancreatic duct, and contains the sphincter of Oddi. This may explain why an ampullary neuroendocrine tumor often clinically manifests as obstructive jaundice or acute pancreatitis, and an attempt to remove the tumor may result in more frequent procedure-related complications [3]. The prognostic significance of tumor size, depth of invasion, and regional lymph node metastases is largely unknown, thus the merits of radical vs. local resection remain uncertain. We report a case of a neuroendocrine tumor of the ampulla of Vater treated by endoscopic snare papillectomy.

Case Report

A 45-year-old female patient presented with right upper and epigastric abdominal pain lasting for 2 months. Results of blood tests were consistent with slightly high pancreatic enzymes (160 U/L) and normal bilirubin levels. A mass appearance was not encountered on contrast-enhanced computed tomography (CT), which revealed dilatation of the common bile duct (CBD) and pancreatic duct (PD). A papilla that was tumor-like macroscopically was seen in the second part of the duodenum in endoscopic retrograde cholangiopancreatography (ERCP) (Figure 1). Biopsies were taken from the ampulla, which was histologically confirmed as a low-grade neuroendocrine tumor without mitosis. Kl-67 was less than 1%. A 1.9×1.6 cm mass was detected on EUS (Figure 2). Prior to papillectomy, the absence of liver metastases and peri-pancreatic lymphadenopathy was confirmed by abdominal ultrasonography, CT, and endosonography (EUS). An In-111 octreotide scan revealed no definitive metastatic lesion. Serum serotonin and urinary 5-HIAA levels were within normal ranges. A chest X-ray was also negative.

Endoscopic snare papillectomy was performed, stents were introduced into the CBD and the pancreatic duct to prevent possible cholangitis and pancreatitis, and no complication were observed in follow-up. Figure 3 shows the endoscopic view of snaring of the carcinoid tumor of the ampulla of Vater, endoscopic view showing the base of the ampulla after papillectomy, biliary and pancreatic stents, and ERCP showing biliary and pancreatic stents. Figure 3A shows the endoscopic view of snaring of the carcinoid tumor of the ampulla of Vater. Figure 3B shows the base of the ampulla after papillectomy, Figure 3C is an endoscopic view of biliary and pancreatic stents, and Figure 3D shows the ERCP of biliary and pancreatic stents.

An ampullectomy specimen was sent as a frozen section to the pathology department for negative resection margins. Figure 4 shows the pathology specimen.

The patient was followed for 14 months and there was no recurrence. The appearance of the ampulla after 12 months is shown in Figure 5.

Pathologic examination revealed a 2×1.5×1 cm tumoral mass that was well-differentiated, low-grade (ENETS G1), and which...
had invaded the submucosa and muscularis propria. There was no mitosis. The specimen was evaluated as a neuroendocrine tumor and stained synaptophysin (+), chromogranin-A poorly (+), and Ki-67 proliferation index was 1% in immunohistochemical staining. Surgical margins were healthy. There was no lymphovascular or perineural invasion.

Adjuvant chemotherapy and biologic treatment were not planned because of the absence of carcinoid syndrome findings and poor prognostic histopathologic properties.

Discussion

Neuroendocrine tumors rarely arise at the ampulla of Vater. Approximately 139 cases have been reported to date, mostly in case reports. Accounting for just 0.05% of all neuroendocrine tumors, it is even rarer than duodenal involvement, which itself is defined as rare (2%). Its clinical presentation consists of jaundice (53.1%), abdominal pain (24.6%), pancreatitis (6.0%), and weight loss (3.6%) [1,4].

Figure 3. Endoscopic snare papillectomy of a neuroendocrine tumor of the ampulla of Vater. (A) Endoscopic view showing snaring of the carcinoid tumor of the ampulla of Vater (B) Endoscopic view showing the base of ampulla after papillectomy (C) Biliary and pancreatic stents (D) ERCP showing biliary and pancreatic stents.
In addition to clinical findings, abdominal tomography and endoscopic imaging methods are also valuable in making a diagnosis. Of the endoscopic imaging methods, endoscopic retrograde cholangiopancreatography, endoscopic biopsy, and endosonographic ultrasonography are especially useful in the diagnosis and detection of invasion depth [4]. Abdominal CT was not helpful for diagnosis of our case, which was diagnosed by ERCP and biopsy.

In our case, careful examinations, including EUS, abdominal CT scan, and ultrasound, were performed before determining the therapeutic options. The tumor size was smaller than 2 cm and there was no evidence of regional lymph node metastasis on EUS. Additionally, most ampullary tumors have been seen to be positive in terms of somatostatin in pathologic examination. Thus, octreotide scintigraphy is used for screening [5]. In-111 octreotide scan performed to evaluate occult metastasis was negative.

In contrast to neuroendocrine tumors of the duodenum, the size of the tumor seems to have no prognostic implications for neuroendocrine tumor of the ampulla of Vater [6]. In a review of 73 cases of neuroendocrine tumors of the ampulla of Vater, in 48% of patients with a tumor larger than 2 cm, it had metastasized, but, interestingly, 40% of patients with tumors less than 2 cm had a metastatic disease [7]. The tumor size was not a reliable predictor of aggressiveness; therefore, complete resection of the tumor is mandatory regardless of size.

Despite frequent regional lymph node metastasis, the prognosis of carcinoid tumors of the ampulla of Vater has generally been considered good. The 5-year survival was 90%, with only 4 (6%) patients dying of a metastatic disease or progressive tumor [1,2]. Some authors state that lymph node dissection does not have a therapeutic effect on ampullary neuroendocrine tumors, and thus recommend local excision or endoscopic resection, which yield lower morbidity and mortality [3,8].

For neuroendocrine tumors with unknown malignant potential, a novel classification system was developed by the World Health Organization. The term carcinoid was replaced with neuroendocrine tumor, which connotes a broader spectrum of histologic appearance and behavior and can be further subcategorized into benign, potentially malignant, and malignant. In this classification, tumor proliferative index, invasion depth, and anatomic location were evaluated. More recently, the European Neuroendocrine Tumor Society (ENETS) proposed a Tumor-Node-Metastasis (TNM) staging and grading system for foregut neuroendocrine tumors [9,10]. Nevertheless, the clinical value of the WHO and ENETS systems as applied to ampullary neuroendocrine tumors is still unproven.

Because of low prevalence, ampullary neuroendocrine tumors still have uncertainties regarding issues like prognostic features, invasion depths, and lymph node metastasis [11]. These uncertainties also affect ampullary neuroendocrine tumor surgical treatment strategy.

The treatment of choice for neuroendocrine tumors of the ampulla of Vater is complete resection, and the standard treatment modality for the tumor has been surgery, such as pancreatoduodenectomy or local excision of the tumor. In a review of 90 cases with an ampullary neuroendocrine tumor, 52 were treated with a pancreatoduodenectomy and 22 with local excision of the tumor. Local excision was generally performed in patients with tumors less than 2 cm in diameter, while a pancreatoduodenectomy was performed in patients with tumors larger than 2 cm. Three of 52 patients who underwent a pancreatoduodenectomy died of postoperative complications, but 21 of the 22 patients who underwent local excision are alive, with no evidence of recurrence after long-term follow-up, and only 1 patient died of local recurrence, 20 months after the local excision [6].

Although a pancreatoduodenectomy enables complete resection of the tumor, this procedure has the disadvantage of...
relatively higher morbidity. Local excision showed satisfactory results in tumors smaller than 2 cm [1]. As a result, local excision may be an option for the treatment of a neuroendocrine tumor of the ampulla of Vater if the tumor is small and there is no evidence of regional lymph node or distant metastasis. Compared to local surgical excision, endoscopic snare papillectomy may be much less injurious to the patient, since it does not require laparotomy and duodenotomy. Endoscopic snare papillectomy is increasingly performed with curative intent for papillary tumors. Complications related to endoscopic snare papillectomy are self-limited. In a recently published article, complications occurred in 18.5% (n=10/54) of cases: bleeding (n=3); pancreatitis (n=7) and perforation (n=1; the only case requiring rescue surgical intervention). There was no intervention-related death (mortality, 0%). For the treatment of tumor lesions of the papilla, a sufficient histopathological investigation is required to achieve an adequate pre-therapeutic tumor staging, which helps in deciding on the appropriate treatment (surgical intervention, papillectomy, or papillotomy) according to the patient's specific finding. These requirements can be fulfilled by endoscopic ultrasonography (EUS) for the majorit of tumor (-like) lesions. For the specific clinical status of the single patient (e.g., high risk because of accompanying diseases) and to cover the need of lower invasiveness and interventional trauma for a more favorable outcome as well as earlier reconvalescence, an additional approach to open surgery (providing transduodenal papillectomy/ampullectomy but with a substantial complication rate) is required – this might be provided by the very specific interventional endoscopic approach termed endoscopic papillectomy [12].

Adjuvant treatment options should be planned by considering prognostic factors of tumor and carcinoid syndrome findings. Adjuvant chemotherapy may be administered following resection in tumors that have poor prognostic factors. The most commonly used agents for chemotherapy are streptozocin, doxorubicin, dacarbazine, and 5-fluorouracil. Other treatment options are biologic therapy (interferon INF and somatostatin analogues SST) and chemoembolization [6,8].

Conclusions

Endoscopic snare papillectomy may be the first step in the management of neuroendocrine tumors of the ampulla of Vater in high-risk surgical candidates and selected patients such as those with a well differentiated, low-grade, tumors smaller than 2 cm in diameter) and without regional/distant metastasis. This technique can also be used for younger patients who want to avoid surgical resection.

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