Endoscopic full-thickness resection of well-differentiated T2 neuroendocrine tumors in the duodenal bulb: a case series

Sarah Dwyer, MS,[1] Shaffer Mok, MD[2]

Background and Aims: Endoscopic therapies have moved to the forefront in the removal of small, well-differentiated duodenal neuroendocrine tumors (NETs). Classic procedures used to address small tumors, especially those less than 1 cm in diameter, are banding without resection, ligation endoscopic mucosal resection, or endoscopic submucosal dissection. Endoscopic full-thickness resection (EFTR) is a procedure developed recently that allows for sealing off of the tissue surrounding the tumor before full-thickness removal. Although surgical resection is typically recommended for NETs measuring 2 cm and larger, this may not always be possible given patients' ages or comorbidities. We present the cases of 3 patients with well-differentiated NETs of the duodenal bulb measuring greater than 2 cm who were poor candidates for surgery and were thus offered EFTR for excision of their tumors.

Methods: Three patients with well-differentiated, stage II NETs of the duodenal bulb underwent chromoendoscopy and narrow-band imaging, EUS, prophylactic dilation of the upper esophageal sphincter and pylorus, and EFTR using an over-the-scope clip system.

Results: In each case, there was no residual mass seen on endoscopy, Ga-68 Dotatate positron emission tomography-CT imaging, or biopsy up to 1 year after the procedure. Two of the 3 cases had normal chromogranin A levels at all follow-up points, and the third case had chromogranin A levels that trended down to a near-normal level of 145 ng/mL.

Conclusions: Three patients with NETs of the duodenal bulb who were poor surgical candidates underwent successful EFTR using a full-thickness resection device. At 1-year follow-up, they have no evidence of disease recurrence on imaging and pathology after EFTR. (VideoGIE 2022;7:196-9.)

Small intestinal neuroendocrine tumors (NETs) are detected with increasing frequency during endoscopy. These tumors are most precisely measured using EUS, which, along with Gallium-68 Dotatate positron emission tomography (PET)/computed tomography (CT) imaging, can help determine stage.[1] Depending on tumor size and characteristics, nonfunctioning NETs may undergo endoscopic resection, local excision with regional lymphadenectomy, or pancreaticoduodenectomy.[2] Localized well-differentiated NETs in the small bowel are increasingly addressed with endoscopic procedures, including banding without resection,[3] endoscopic mucosal resection, and endoscopic submucosal dissection, but these procedures incur significant risks including bleeding and inconsistently produce negative margins.[1]

Endoscopic full-thickness resection (EFTR) is a minimally invasive endoscopic procedure that allows for potentially curative treatment in local disease.[4] There are limited data regarding the use of EFTR for duodenal NETs, although several studies have reported consistent negative margins, with 2 of 3 studies noting no adverse events (AEs).[4-6] Potential AEs of EFTR include perforation, microperforation, and hemorrhage.[6] This approach is most often used for localized, subcentimeter, well-differentiated NETs, whereas surgical resection is generally recommended in tumors >2 cm.[7]

CASE DESCRIPTION

Here, we describe the cases of 3 patients with well-differentiated stage II, grade G1 NETs of the duodenal bulb who, because of age and comorbidities, were determined to be poor surgical candidates (Video 1, available online at GIEjournal.org).

After obtaining serologic markers and Ga-68 Dotatate PET/CT imaging showing no nodal involvement or distant metastatic disease, each case was discussed in a multidisciplinary neuroendocrine tumor board with medical oncology, surgical oncology, pathology, radiology, and

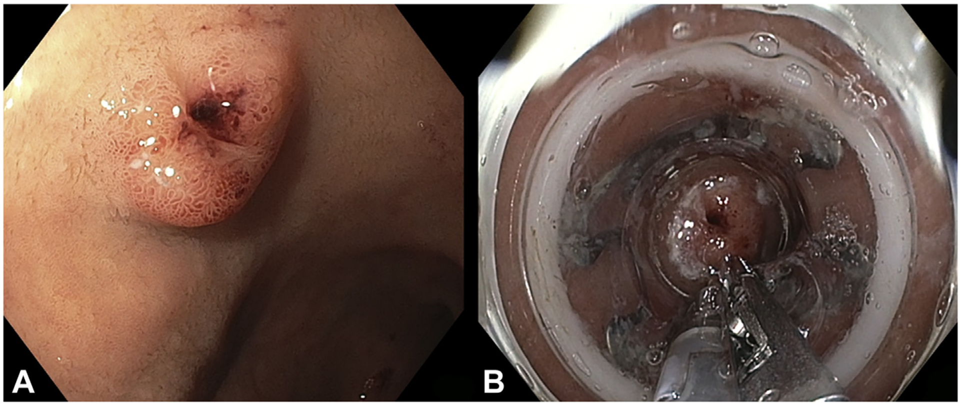

Figure 1. A, Stage II well-differentiated neuroendocrine tumor in the duodenal bulb. **B,** Grasping tool pulling tumor into the cap of the over-the-scope bear claw clip system before clip was deployed.

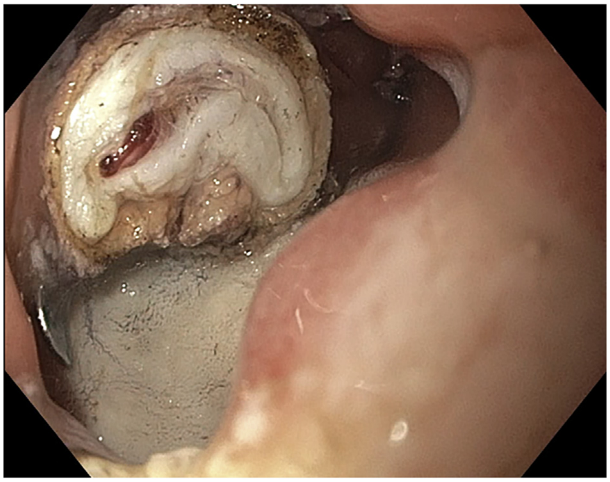

Figure 2. Immediately after deployment of the bear claw clip and snare at high cutting currents.

therapeutic endoscopy. The consensus was to recommend EUS (Olympus GF-UE160-AL5, Center Valley, Penn, USA) and possible endoscopic resection of the masses. EUS showed tumors measuring >20 mm in dimension and involvement of the lesion into the submucosal layer, staging these as T2N0M0,[2] American Joint Committee on Cancer stage II.[8] Given the endoscopic, histologic, and radiologic findings and discussion with a multidisciplinary tumor board, the decision was made to proceed with EFTR.

Patient 1 was an 81-year-old man with comorbidities including chronic obstructive pulmonary disease (COPD), pulmonary hypertension, and coronary heart failure who had a 25-mm tumor with initial serum chromogranin level of 436 ng/mL. His tumor was positive for gastrin and chromogranin A, weakly positive for CDX2, and Ki67 2%.

Patient 2 was a 78-year-old man with comorbidities including COPD, coronary heart failure, and atrial fibrillation who had undergone multiple previous abdominal surgeries. His tumor was 22 mm in size with a serum chromogranin A level of 345 ng/mL. His tumor was positive for gastrin and chromogranin A, weakly positive for CDX2, and Ki67 2%.

Patient 3 was a 77-year-old woman with comorbidities of COPD on home oxygen and severe aortic stenosis who had a 20-mm tumor and initial serum chromogranin A level of 398 ng/mL. Her tumor was positive for gastrin and chromogranin A, weakly positive for CDX2, and Ki67 2%.

PROCEDURE

Patients did not receive periprocedural antibiotics, were not admitted, and required no upper GI series after this procedure. After visualization and staging, each patient underwent upper endoscopy using a therapeutic endoscope (Olympus GIF-2TH180) under high-definition white light, narrow-band imaging, and methylene blue chromoendoscopy, demonstrating the mucosal mass. Narrow-band imaging and methylene blue chromoendoscopy highlight tissue architecture and aid in determining borders of the lesion, which can be very subtle. Because the EFTR full-thickness resection device (FTRD) (Ovesco Endoscopy AG, Tübingen, Germany) is 19.5 mm in diameter, the upper esophageal sphincter and pylorus were dilated with an 18-19-20-mm balloon (CRE Wire-guided Balloon Dilator, Boston Scientific Corporation, Boston, Mass, USA). Next, the borders of the mass were marked with EFTR probe. The EFTR grasping tool was used to pull the lesion into the cap of the FTRD for EFTR (Fig. 1). The FTRD bear claw clip and snare were deployed with high cutting current settings (Fig. 2). Figure 3 demonstrates the deployment of the FTRD. We do not use suction during this procedure because it puts the lesion at an oblique angle with a higher risk of perforation. EFTR resulted in negative margins in all cases.

After the procedure, patients were placed on clear liquid diets for 24 hours, then full liquid diets for 24 hours,

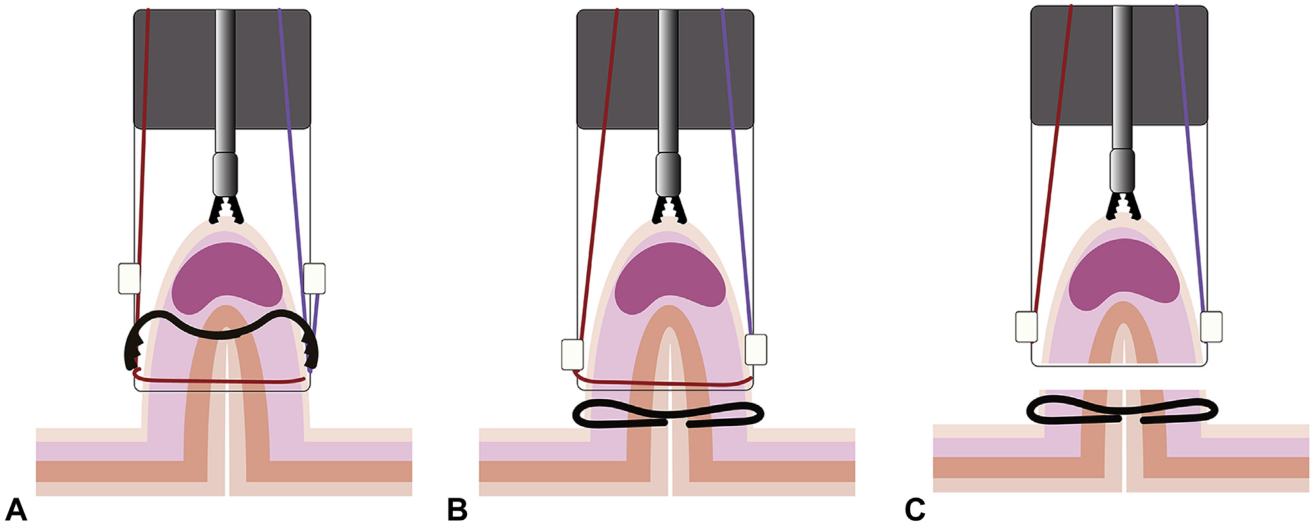

Figure 3. Schematic showing grasping tool pulling mass into the cap of full-thickness resection device **(A),** deployment of over-the-scope bear claw clip **(B),** and full-thickness resection of mass using the snare **(C)**.

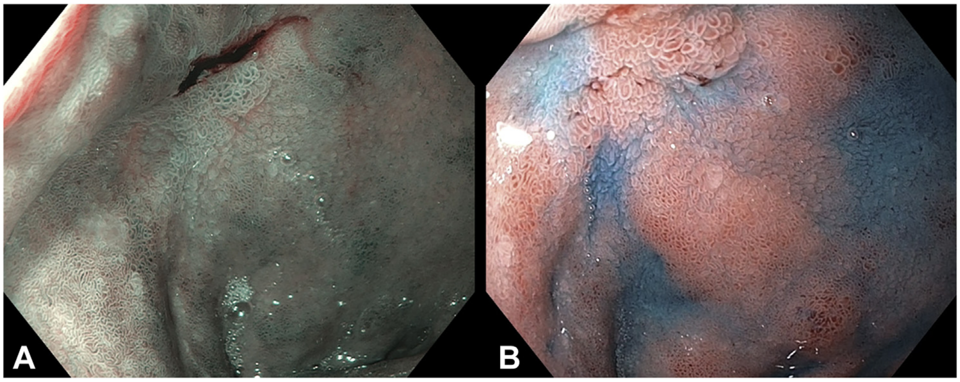

Figure 4. Site of resection 3 months after the procedure, visualized with narrow-band imaging **(A)** and methylene blue chromoendoscopy **(B),** with visible scar. In this case, the clip was not retained.

followed by pureed diet for 3 days. They also received a full-dose proton pump inhibitor twice daily and sucralfate every 6 hours for 8 weeks. Every 3 months after the initial procedure, each patient received surveillance endoscopy and biopsy (Captura Pro Biopsy forceps, Cook Medical, Bloomington, Ind, USA).

OUTCOMES

In all cases, EFTR was successfully used to resect the well-differentiated, stage II NETs, and R0-resection was achieved. There was no evidence of disease recurrence by Ga-68 Dotatate PET/CT imaging or pathology up to 1 year after the procedure. In 2 of the 3 cases, the clip was not retained and there was a visible scar (Fig. 4). Two of the 3 cases had normal chromogranin A levels at all follow-up points, and the third case had chromogranin A levels that have trended down to 145 ng/mL compared with a normal level of less than 140 ng/mL.

Although EFTR was successfully used in these 3 cases without any AEs, limitations of this technology may include the possibility of grabbing extraintestinal structures including the gastroduodenal artery, bile ducts, or loops of bowel. Therefore, EUS preceding EFTR is paramount to measure distance between the lesion and these structures. Moreover, there is a risk of perforation if the over-the-scope clip misdeploys in an oblong manner; however, using the grasper tool to pull the tissue into the cap rather than using suction limits this risk.

CONCLUSIONS

We have demonstrated successful R0 resection without AEs or endoscopic, radiologic, or histologic evidence of recurrence of well-differentiated duodenal NETs >2 cm in 3 patients who were poor surgical candidates using EFTR. Based on these findings, EFTR appears to be a viable option for removal of grade G1, stage II duodenal NETs in patients who are poor surgical candidates.

DISCLOSURE

Dr Mok is a consultant for Medtronic and ConMed. All other authors disclosed no financial relationships.

Abbreviations: AE, adverse event; COPD, chronic obstructive pulmonary disease; CT, computed tomography; EFTR, endoscopic full-thickness resection; FTRD, full thickness resection device; NET, neuroendocrine tumor; PET, positron emission tomography.

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Geisinger Commonwealth School of Medicine, Scranton, Pennsylvania (1), Moffitt Cancer Center, Tampa, Florida (2).

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