

CASE REPORT

십이지장 신경절세포 부신경절종의 내시경 절제술: 4예 보고

박세정, 김도훈, 임 현, 이정훈, 최기돈, 송호준, 이진혁, 정훈용, 김진호, 박지영¹

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Endoscopic Resection as a Possible Radical Treatment for Duodenal Gangliocytic Paraganglioma: A Report of Four Cases

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Gangliocytic paraganglioma (GP) is a rare, benign tumor which is usually found in the duodenum. We here report four recent cases of GP, with successful endoscopic resection in three cases, including a lesion on the ampulla of Vater. In all cases, each lesion had a stalk that facilitated removal using an endoscopic approach. Endoscopic mucosal resection is a feasible and safe treatment if the location, depth, and lymph node status are all favorable and is also helpful for definite diagnosis of unknown duodenal mass. To avoid morbidity resulting from open surgical resection, careful inspection for the peduncle of the GP will help determine the feasibility of endoscopic resection. (*Korean J Gastroenterol* 2014;63:114-119)

Key Words: Paraganglioma; Duodenum

INTRODUCTION

Gangliocytic paraganglioma (GP), a rare, poorly understood, benign tumor, usually occurs in the second portion of the duodenum. Approximately 190 cases have been reported since it was first described as a 'duodenal ganglioneuroma' in 1957.¹ Disease prognosis is favorable with no recurrence after surgical resection, despite 17 reported cases of GP with regional lymph node metastases. Surgical resection is the most common treatment for GP, with reports of 15 patients who underwent endoscopic removal² and one patient who underwent radiotherapy after surgery.³ GP can only be cured by endoscopic resection or use of a limited surgical technique, such as local excision without pan-

creaticoduodenectomy, the latter of which is associated with significant morbidity and mortality.

We have identified four cases of GP at our institution over the past three years; three of these patients were treated with endoscopic resection only. The current report provides a description of these cases of GP and an evaluation of their associated clinical, endoscopic, and pathologic features in terms of feasibility of endoscopic resection.

CASE REPORT

1. Case 1

A 56-year-old woman was referred for evaluation after detection of a duodenal mass during esophagogastroduodeno-

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scopy (EGD) performed for evaluation of dyspepsia.

CT showed a mass measuring 2.9 cm at the medial aspect of the second portion of the duodenum, which showed subtle hypervascularity in the arterial phase. The features were suggestive of a duodenal gastrointestinal stromal tumor or a neuroendocrine tumor, with no evidence of local or bile duct dilatation. Endoscopy showed a subepithelial tumor measuring 3 cm with ulceration and a stalk just proximal to the ampulla of Vater (AoV) in the second portion of the duodenum (Fig. 1A). EUS showed a well-circumscribed, inhomogeneous, hypoechoic mass with a layer of origin that was barely identifiable due to the long stalk. Snare polypectomy was performed successfully for removal of the lesion. Tumor histology revealed GPs with synaptophysin (+), CD56 (+), and S-100 protein (+), with clear resection margins (Figs. 2, 3). No evidence of recurrence was observed on follow-up EGD after six months.

2. Case 2

A 56-year-old woman was referred for a work-up to address anemia reported at another hospital. No specific abnormality was found on EGD and colonoscopy; however, abdominal CT showed a pedunculated mass measuring 4.3 cm with intussusception of the second section of the duodenum into the jejunum. CT indicated a duodenal villotubular adenoma with cancer foci. The patient was referred to our hospital, where we performed double balloon enteroscopy via an oral approach. A huge lobulated mass with ulceration was found, spanning from the second portion of the duodenum to the jejunum. The lesion may have originated from the periampullary area, however, the site was difficult to identify from the ampulla because of the very large stalk. Snare polypectomy was attempted first; however, this approach failed because the stalk was too large to be caught by the snare. Transduodenal ampullectomy was subsequently performed just beneath the ampullary orifice of the common duct. A bipolar-shaped, smooth-surfaced, soft mass measuring 5×3 cm with a stalk measuring 5 cm was identified. The final pathologic results showed a GP that stained positive for synaptophysin, chromogranin, and S-100 protein. The patient has been followed for 30 months after surgery without recurrence on CT.

3. Case 3

A 46-year-old woman was referred to our hospital due to a mass of the AoV. She reported no gastrointestinal symptoms. EGD showed an enlarged papilla with a granular and papillary surface (Fig. 1C). The first endoscopic impression was that of an AoV cancer. Biopsy showed only inflammation with fibrosis and no tumor mass. CT and MRI were also performed, but showed no definite mass at the AoV or any dilatation of the bile duct. On suspicion of malignancy, we performed an ampullectomy and placed a plastic stent in the pancreatic duct in order to prevent acute pancreatitis. Histological findings indicated GP with a clear resection margin. The patient has been followed for 23 months after the tumor endoscopic resection and an annual EGD has shown no recurrence.

4. Case 4

A 70-year-old man was referred to our hospital due to a duodenal mass found during an EGD performed as part of a health screen (Fig. 1D). EUS showed a hypoechoic mass measuring approximately 2 cm proximal to the AoV in the second portion of the duodenum with heterogenic internal echo and a duct-like structure suggestive of ectopic pancreas or Brunner's gland hyperplasia. CT showed a well enhancing mass with a peduncle and no enlarged lymph node was observed. Snare polypectomy was performed. Histology showed a GP with a clear resection margin. The patient was followed for one year after surgery without recurrence on EGD.

DISCUSSION

We reported here on four cases of GP, an extremely rare, benign tumor. Three of the four tumors were completely resected by endoscopy. These tumors are slightly more common in males (M : F=114 : 76 to 6 : 1)⁴ and the mean age at diagnosis is 52.6 (range, 15-84).² Gastrointestinal bleeding (45.1%) was reported as the most common symptom at presentation, followed by abdominal pain (42.8%) and anemia (14.5%),² and some cases were identified incidentally.⁵ In this report, one patient presented with abdominal pain, one with anemia, and two cases were found during an asymptomatic annual check-up endoscopy.

In terms of endoscopic features, approximately 90% of

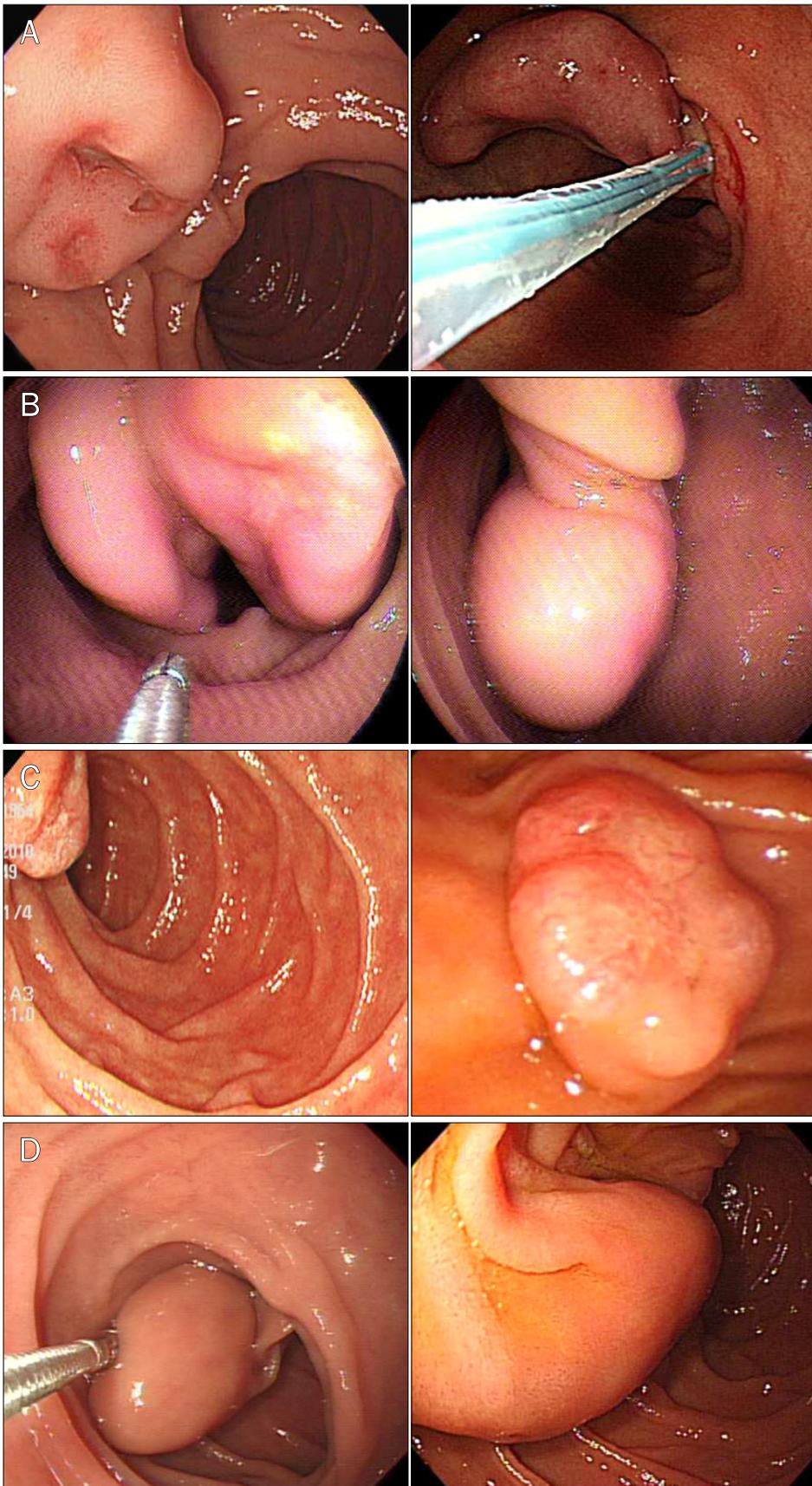


Fig. 1. (A) Case 1. Endoscopic view of the duodenal tumor with an ulcerated surface and stalk. (B) Case 2. Huge duodenal mass with a large stalk. (C) Case 3. Duodenoscope side view showing a short stalk. (D) Case 4. Endoscopic view of the subepithelial tumor of the duodenum with a stalk.

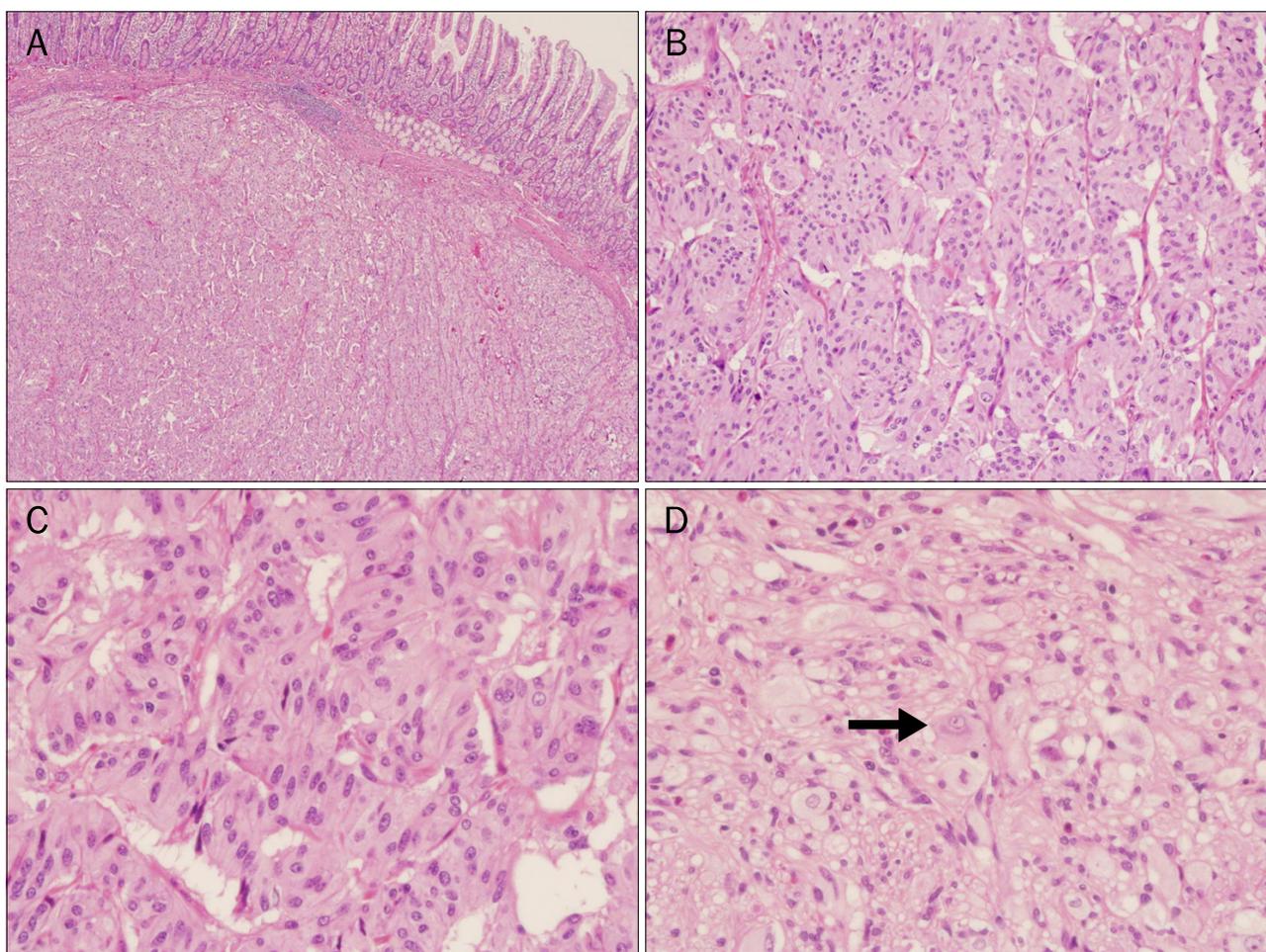


Fig. 2. Photomicrographs showing key features of the gangliocytic paraganglioma in case 1 (H&E). (A) Epithelioid cell nests are located in the submucosal area ($\times 40$). (B) Epithelioid cells are arranged in nests or trabeculae ($\times 100$). (C) Epithelioid cells are large, polygonal or fusiform with an abundant eosinophilic granular cytoplasm ($\times 400$). (D) The ganglion cells (arrow) are scattered throughout ($\times 400$).

GPs are localized to the second portion of the duodenum near the ampulla of Vater. In previous reports,^{3,5,6} GPs varied in size, from 0.5-10 cm, which is similar to our current report, where tumors ranged from 0.5-4.3 cm. Endoscopic features of GPs, such as ulcerations and the presence of a peduncle are also present on other types of submucosal tumors of the duodenum.⁶ Although the reported GP diagnostic rate by endoscopic biopsy is only 11.4%,² endoscopic biopsy for histologic identification can be difficult because of its submucosal nature.

Histological differential diagnosis of GP includes conventional paraganglioma, a well-differentiated neuroendocrine tumor (carcinoid tumor), and solitary ganglioneuroma.⁷ The characteristic triphasic pattern is the most important diagnostic feature and is usually sufficient to exclude other potential entities.⁷ All cases were typical examples of GP and

showed fundamentally similar histopathologic features. The four tumors were not encapsulated and were centered in the submucosa.

Due to the possibility of metastasis or recurrence, some investigators have suggested radical resection, such as pancreaticoduodenectomy with lymph node dissection, for large lesions. However, the Whipple procedure is associated with a perioperative mortality rate of approximately 4% and complication such as bile leak or delayed gastric emptying. Although the possibility of lymph node involvement still exists, GP is usually benign, such that simple local surgical resection or endoscopic removal is sufficient in most cases. However, there is still concern regarding lymph node metastasis or recurrence. There was no obvious evidence for an association between GP size and lymph node metastasis. The mean tumor size with lymph node metastasis was 3 cm

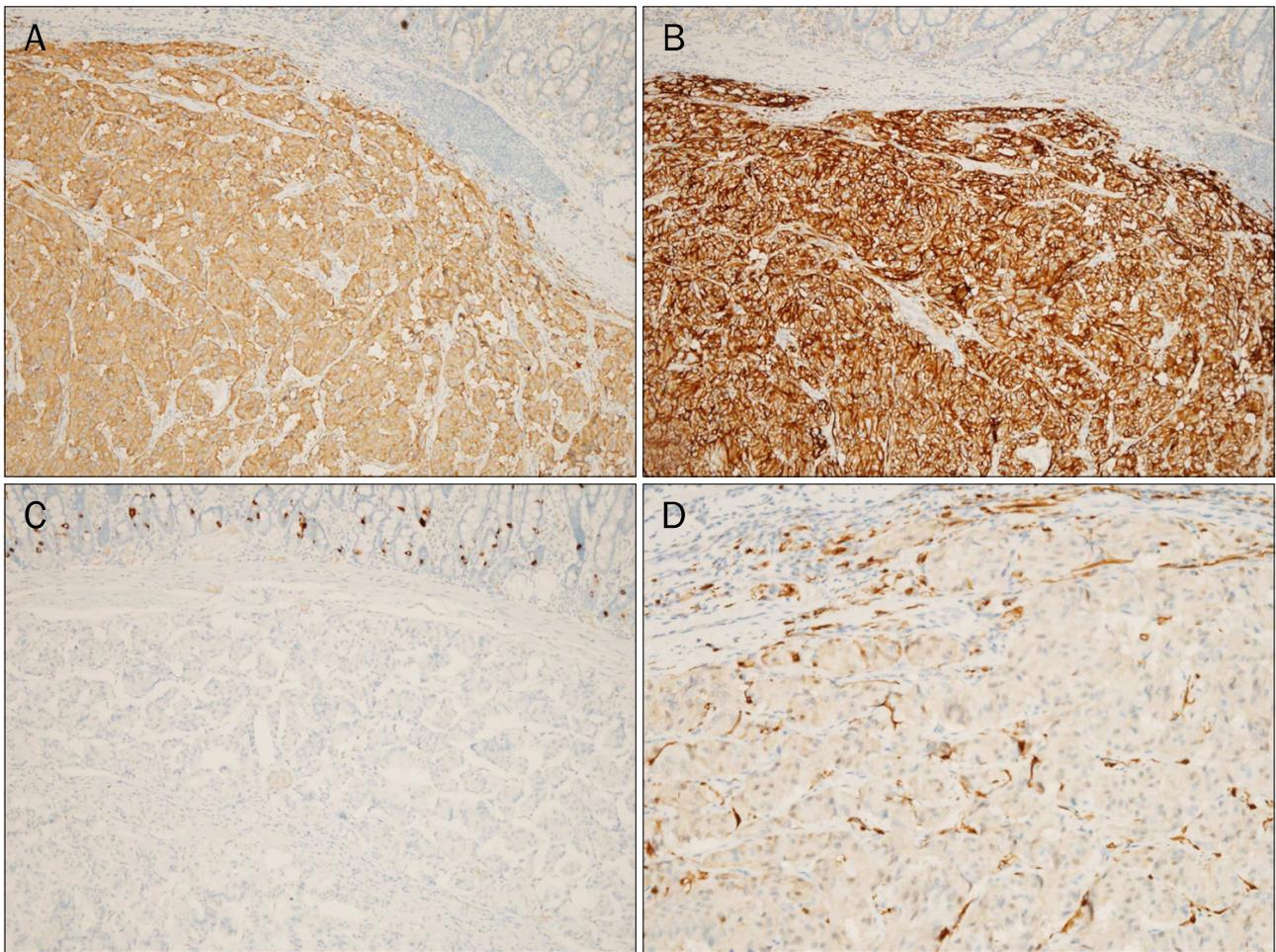


Fig. 3. Photomicrographs showing representative immunohistochemistry of the gangliocytic paraganglioma in case 1. (A) Epithelioid cells showed positive staining for synaptophysin ($\times 200$). (B) Epithelioid cells showed positive staining for CD56 ($\times 200$). (C) Epithelioid cells are negative for chromogranin ($\times 200$). (D) Spindle cells encompassing the epithelioid nests are highlighted by S-100 protein ($\times 200$).

(range, 1.4-6.5 cm), which was similar to the mean tumor size without lymph node metastasis (2.5 cm, range 0.5-10 cm).² Previous GP treatment algorithms based on tumor size and lymph node status have proposed that endoscopic removal could be considered if the tumor is small (< 2 cm) with no evidence of peritumoral lymph nodes on CT scan.⁴ In terms of tumor size, we suggest that tumors larger than 2 cm can be treated with endoscopic resection. Previous reports have confirmed that endoscopic resection for GP larger than 2 cm can be performed without complication,^{8,9} with the largest reported tumor measuring 4 cm in size.¹⁰ We reported on three cases with tumors measuring 0.5, 2.9, and 3.1 cm in size, all of which were treated successfully with endoscopic resection. If a tumor appears to be pedunculated, endoscopic resection can be performed using a method such as endoloop ligation, which helps to prevent perforation. Among our cases, all four

lesions were located in the dependent portion of the duodenum. This location made ready identification of a tumor stalk difficult, however, careful endoscopic examination using a side view duodenoscope (TJF-240; Olympus Co. Ltd., Tokyo, Japan) or forceps revealed stalks that facilitated easy removal using an endoscopic approach. With improvements in endoscopic techniques, we suggest that resection of GPs with sizes much greater than 2 cm can be achieved using endoscopic methods, especially when they are clearly pedunculated. In order to minimize the risk of lymph node metastasis or recurrence, pre procedural imaging study such as CT scan and EUS should be performed and careful histologic examination of features predicting malignant potential, such as nuclear pleomorphism, mitotic activity, and infiltrative margin is suggested after endoscopic or surgical local resection.¹¹ In addition, long term follow-up is suggested due

to the possibility of recurrence. Because this endoscopic resection is relatively safe and simple when compared with surgical resection, it is also helpful for definite diagnosis of an unknown duodenal mass.

We performed successful endoscopic resection in three cases, including a lesion on the ampulla of Vater. Although metastatic GP involvement of regional lymph nodes has been reported, endoscopic mucosal resection is a feasible and safe treatment if the location, depth, and lymph node status are all favorable. In addition, careful inspection for a GP peduncle may be helpful in determining the feasibility of endoscopic resection, thus avoiding the potential morbidity associated with open surgical resection.

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