Gastric Heterotopic Pancreas Can Be Identified by Endoscopic Direct Imaging with Submucosal Endoscopy

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INTRODUCTION

Heterotopic pancreas (HP) in the stomach is a rare pathological entity that poses a challenge for clinical diagnosis and management. Heterotopic pancreas is a benign submucosal tumor (SMT). The majority of patients with HP are asymptomatic, although a minority of patients may present with a variety of symptoms, most commonly epigastric pain [1]. The histological diagnosis of HP is generally difficult when tissue samples are obtained using biopsy forceps [2]. Therefore, surgery [1, 3] or endoscopic resection [4, 5] is sometimes performed in cases of HP as a result of tissue sampling error. Endoscopic ultrasonography (EUS) was reported to aid the diagnosis of HP [6]. However, it is difficult to morphologically distinguish the different types of SMTs by EUS [7, 8]. Recently, EUS-guided fine needle aspiration (FNA) has emerged as an important method for SMT diagnosis [9]. However, because this technique provides limited diagnostic accuracy due to the limited amount of tissue that can be collected, an improved method for tissue sampling is needed.

TECHNIQUE

We previously developed and demonstrated the usefulness of bloc biopsy using submucosal endoscopy with a mucosal flap (SEMF) method as a novel method for collecting tumor tissue under direct vision to assist in the diagnosis of SMTs [10-12]. The SEMF method [10] with the ESD technique was developed to permit a safer offset entry into the peritoneal cavity for natural orifice transluminal endoscopic surgery (NOTES) [13]. This technique comprises five major procedures: endoscopic
submucosal dissection (ESD) procedure, SEMF, bloc biopsy to acquire a specimen of sufficient size (~5 mm), long attachment method for tissue collection, and clip closure from the tumor side. One technical advantage of bloc biopsy using SEMF is that once the submucosal dissection is completed, creating a tunnel into the submucosa toward the tumor, the tumor can be visually identified, enabling the reliable collection of tumor tissue. This method permits the direct visualization and endoscopic imaging of the tumor; these images can then be used to assess the macroscopic characteristics of SMTs, including the color, smoothness, and softness of the tumor surface. Therefore, bloc biopsy using SEMF permits endoscopic direct imaging (EDI) of SMTs in the submucosa via a dissected submucosal tunnel (Fig. 1). To the best of our knowledge, this is the first report to characterize the EDI findings of HP among SMTs.

**Case Reports**

**Case 1**

A 66-year-old woman was admitted to our hospital for further examination of a gastric SMT (diameter, 16 mm) located in the anterior antrum (Fig. 2A). Computed tomography (CT) revealed an enhanced mass measuring 16×12 mm in the lower area of the stomach (Fig. 2B). EUS revealed a lesion of 16 mm in diameter, with low and high complex echogenicity around the tissue, originating within either the submucosa (SM) or muscularis propria (MP) layers (Fig. 2C), consistent with a suspected gastrointestinal stromal tumor (GIST). EUS-FNA biopsy failed to accurately diagnose the SMT due to an inadequate tissue sample. Typically, laparoscopic wedge excision of the lesion would be the procedure of choice. However, we recommended bloc biopsy with SEMF as a less invasive method of obtaining a tissue sample. Informed consent was obtained from the patient as required by our Hospital Clinical Ethics Committee. The SEMF method was used to create a short tunnel via additional submucosal dissection to access the tumor, and EDI through the dissected submucosal tunnel revealed a soft yellow tumor with a multi-nodular surface identified as pancreatic tissue (Fig. 2D). We strongly suspected that the SMT was an HP based on the EDI findings. No complications, such as bleeding requiring blood transfusion or perforation, occurred during or after the procedures. Histopathological findings by bloc biopsy with SEMF revealed excretory ducts and acinar cells, confirming the diagnosis of gastric HP (Fig. 2E).

**Case 2**

A 49-year-old woman presented with a growing SMT (diameter, 15 mm) located in the anterior middle body of the stomach (Fig. 3A). A CT scan revealed an enhanced mass measuring 15×13 mm in the mid-body of the stomach. EUS revealed a lesion 15 mm in diameter that exhibited a mosaic pattern and originated in the SM layer. EUS-FNA biopsy failed to accurately diagnose the SMT because of the stiffness of the device, which prevented deep insertion of the needle. After obtaining informed consent, we performed bloc biopsy with SEMF to obtain a tissue sample from this patient. A 10-mm opening flap was created by a mucosal incision and cutting using ESD (Fig. 3B). After an additional submucosal dissection in front of the tumor using SEMF, EDI revealed tissue with a yellowish, multi-nodular appearance that was subsequently identified as pancreatic tissue (Fig. 3C). We strongly suspected that the SMT was an HP based on the EDI findings. The patient had no complications. Histopathology by bloc biopsy with SEMF confirmed the diagnosis of gastric HP (Fig. 3D).
DISCUSSION

In this initial experience with EDI acquired by bloc biopsy using SEMF, we found that endoscopic visualizations of gastric HP via a dissected submucosal tunnel revealed a yellowish multi-nodular mass identified as pancreatic tissue. Thus, this approach appears to be promising, with potential diagnostic value in distinguishing HP and SMTs.

Symptomatic (obstructive or hemorrhagic) HP requires surgery to relieve symptoms [14]. However, the preoperative diagnosis for asymptomatic HP is important due to the different therapeutic approaches; asymptomatic HP is a benign lesion that can be followed long-term without further intervention. Traditionally, surgery [1, 3] or endoscopic resection [4, 5] is performed in cases of HP because of the difficulty of obtaining a definitive preoperative diagnosis. Heterotopic pancreas is most often detected as an incidental finding during routine upper endoscopy. The typical endoscopic finding is a firm round or oval subepithelial lesion with a central depression, which corresponds to the opening of a duct [15]. In this study, because the HPs were both surrounded by normal surfaces, routine upper endoscopy was not helpful for diagnosis.

Recent studies have reported the utility of EUS and EUS-FNA in the preoperative diagnosis of HP [6, 9]. EUS is a key procedure in the evaluation of SMTs of the gastrointestinal (GI) tract. The characteristic EUS features of HP, including indistinct margins, heterogeneous echogenicity (mainly hypoechoic, accompanied by scattered small hyperechoic areas), the presence of an anechoic area and fourth-layer thickening, and location within the second, third, and/or fourth layers, are useful for establishing a preoperative diagnosis of HP [15]. However, the identification of morphologic features by EUS alone has limited utility in diagnosing the diverse subtypes of SMTs [7, 8]. Recently, Fujii et al reported that EUS-FNA was helpful for diagnosing HP [16]. However, in the two HP cases in the present study, the tissue sampling error by EUS-FNA suggests that EUS-FNA may be limited in the diagnosis of HP. Technical failure may be secondary to the difficulty of endoscopic handling and stroke in small tumors (2 cm in diameter). Further studies are needed to confirm the efficacy of EUS-FNA for tissue sampling in HP.

We previously demonstrated the safety and usefulness of bloc biopsy using SEMF as a novel method for collecting tumor tissue under direct visualization to assist in the diagnosis of SMTs [10-12]. In all eight cases in the current study, this technique provided accurate diagnoses and induced no complications, such as bleeding requiring blood transfusion or perforation, during or after the procedures [12]. Using this method, which provides direct visualization of the tumor, endoscopic images of the tumor can be obtained and can then be used to assess the macroscopic characteristics of the SMTs, including the color and softness of the tumor surface. In the two HP cases in the present study, the tumors were yellow and soft, and the tumor surfaces were multi-nodular with the appearance of pancreatic tissue. Macroscopically, HP appears as a lobular white or yellow nodular tumor [17]. In contrast, a typical GIST image is macroscopically characterized as a hard, globular, gray-white tumor. However, the specificity of the endoscopic characteristics of SMTs has not been rigorously evaluated. SEMF permits the EDI of SMTs in the submucosa via a dissected submucosal tunnel. Therefore, this study suggests that EDI findings characteristic of HP may enable physicians to distinguish HP from other SMTs and that EDI may help to avoid unnecessary operations on gastric submucosal lesions. However, the present study has several weaknesses, including its retrospective nature and the small sample size. Therefore, larger, prospective, and comparative studies are required to confirm its superiority in this setting.

CONCLUSIONS

This study illustrated that endoscopic visualization of gastric HP via a dissected submucosal tunnel revealed characteristic EDI findings, a yellowish multi-nodular mass identified as pancreatic tissue. EDI findings may help to avoid unnecessary operations on gastric HP. The clinical usefulness of the current diagnostic techniques could lead to new diagnostic criteria based on EDI.

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REFERENCES