CASE REPORT

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Submucosal Endoscopic Sampling for Indefinite Gastric Linitis Plastica Infiltrating into the Submucosal Layer

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ABSTRACT

The diagnosis of diffuse-type gastric cancer, named linitis plastica (LP), is difficult because of its infiltration into the submucosa. Conventional endoscopic biopsy sampling may show false-negative results because the superficial mucosa is often normal. These macroscopic features do not often permit the distinction between benign and malignant lesions, and sampling methods have some limitations. Accordingly, a secure sampling method is required in order to increase the diagnostic yield. We have developed a submucosal tunneling technique for sampling submucosal tumors, which can visualize tumor surfaces and obtain tissue samples under direct vision. We report a rare case of indefinite gastric LP that could be diagnosed by this method. As multiple biopsies and endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA) did not help us histologically diagnose the lesion, our new method of submucosal endoscopy which has advantages of visualizing tumor surfaces and obtaining tissue samples under direct vision in the submucosa was introduced. Histological examination of all acquired samples confirmed the presence of a poorly differentiated adenocarcinoma. The present case demonstrates that this method is a reasonable option for indefinite LP with features inflating into submucosa, providing an update on the contemporary concepts.

Key words: gastric linitis plastica – tissue sampling method – submucosal endoscopy.

Abbreviations: ESD: endoscopic submucosal dissection; EUS-FNA: endoscopic ultrasound (EUS)-guided fine needle aspiration; LP: linitis plastica; NOTES: natural orifice transluminal endoscopic surgery; POEM: natural orifice transluminal endoscopic surgery; SEMF: submucosal endoscopy with a mucosal flap safety valve.

INTRODUCTION

Linitis plastica (LP) is a diffuse infiltrative gastric adenocarcinoma and is characterized by thickened folds and fibrosis of the gastric wall [1]. A number of diseases may present with thickened gastric folds including malignant tumors (adenocarcinoma, lymphoma) as well as benign diseases (Menetrier's gastritis, amyloidosis, and lymphoid hyperplasia) and the therapeutic management of these diseases is clearly different. However, in the case of malignancy, the gastric mucosa is frequently spared malignant invasion and conventional endoscopic biopsy sampling frequently shows false-negative results [2]. In addition, a delayed diagnosis can lead to a poorer prognosis due to the aggressive nature of these tumors [3]. Because of this, it is very important to make a definitive diagnosis promptly and accurately. We have developed recently a tissue sampling method using a submucosal tunneling technique for submucosal tumors [4, 5].

One technical advantage of this method is that once a small opening flap is made by using the endoscopic submucosal dissection (ESD) technique, creating a tunnel into the submucosa towards the tumor, the tumor can be visualized through the submucosal tunnel, enabling the secure acquisition of tissue sample. Among the new endoscopic interventions is the submucosal tunneling technique, which involves the introduction into the submucosa of tunnels that permits a safer offset entry into the peritoneal cavity for natural orifice transluminal endoscopic surgery (NOTES) [6]. The method is the first that the group from the Mayo Clinic described as submucosal endoscopy with a mucosal flap safety valve (SEMF) [7]. This method, known as per oral endoscopic myotomy (POEM) for patients with achalasia, has opened up a new discipline of submucosal endoscopic surgery [8]. Currently, other clinical applications of the submucosal tunneling

technique include its use in the removal of gastrointestinal subepithelial tumors [9].

CASE PRESENTATION

A 78-year-old woman with anorexia underwent upper gastrointestinal (GI) endoscopy and X-ray examination, which revealed circumferential thickening and rigidity of the gastric wall localized to the gastric body, with normal extensibility of the antrum and fornix (Fig.1A, 1B). EUS demonstrated a homogeneous hypoechoic lesion infiltrating into the submucosa. Positron emission tomography-CT showed atypical pale staining localized to the gastric wall of the body of the stomach. Twenty-one biopsy samples were acquired from the thickened gastric folds during three endoscopic examinations to establish a diagnosis. However, multiple biopsies and EUS-FNA did not help us histologically diagnose the lesion.

After informed consent was obtained, we proceeded with the submucosal biopsy as we previously described [4, 5]. First, a mucosal incision based on the ESD technique was performed to create a 10-mm opening flap (Fig. 2A), followed by 2-point marking of the normal antral mucosa around the lesion with 10 mm margins. Next, a submucosal tunnel was created with submucosal dissection toward the thickened walls. At this point, through the submucosal tunnel, we could visualize a soft whitish mass surrounded by fibrotic tissues (Fig. 2B). Subsequently, three tissue samples were acquired using biopsy forceps (Radial Jaw™ 4 Standard Capacity; Boston-Scientific, Tokyo, Japan). Finally, several vessels visualized in the submucosa were cauterized using hemostatic forceps (Coagrasper, FD-410 LR; Olympus, Tokyo, Japan). The patient had no procedure related adverse events. Histological examination of all acquired samples confirmed the presence of a poorly differentiated adenocarcinoma. Histological examination after total gastrectomy revealed a rare case of gastric LP inflitrating into the deep submucosa with a remarkable fibrosis of the muscularis propria and serosa.

DISCUSSION

Linitis plastica is a gastric cancer of diffuse histotype that presents in the fundic gland area, and is featured by poorly differentiated tumor cells that diffusely infiltrate the gastric wall, thus leading to reactive fibrosis. At early stage, LP-type gastric cancer appears as a depressed type of lesion in the epithelium of the gastric wall, progressing by diffuse infiltration into the submucosal layer prior to ulceration of the primary lesion, with the cancer cells extending beyond the fibrous tissue [10]. Although the invasion and spread of LP-type gastric

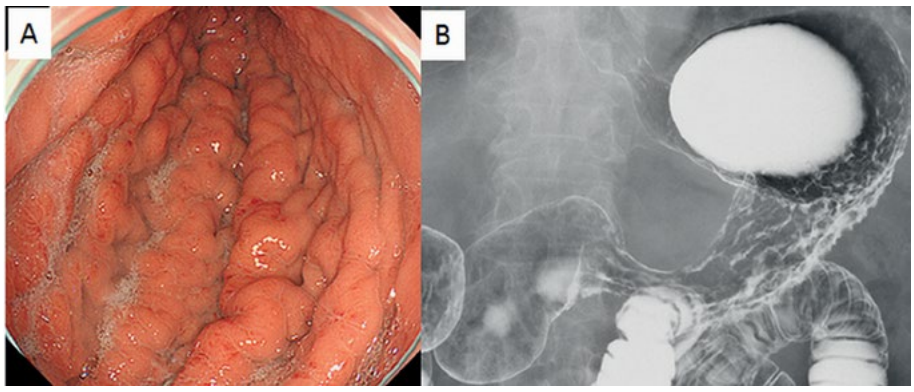

Fig. 1. A. Endoscopic findings showing circumferential thickening and rigidity of the gastric wall localized at the gastric body. B. Upper GI radiographs showing the entire stomach with localized rigidity of the wall of the gastric body without rigidity of the walls of the antrum and fornix.

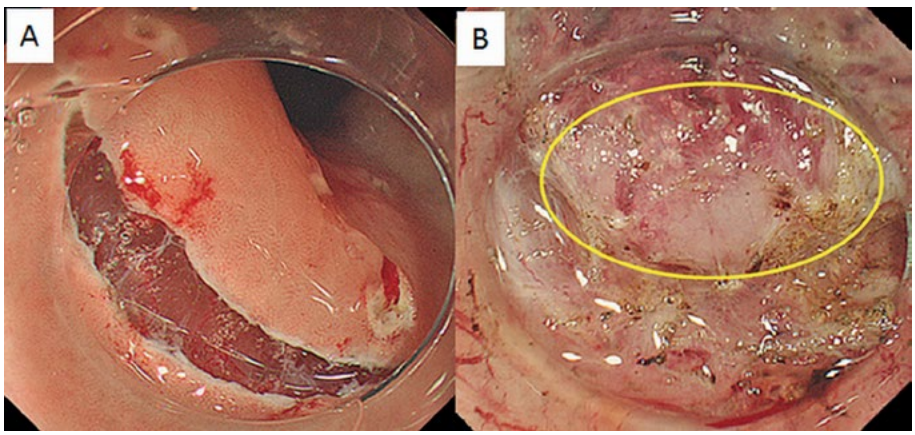

Fig. 2. A. Endoscopic retroflex view showing a 10-mm opening flap created after marking the normal antral mucosa around the lesion with 10-mm margins. B. Endoscopic findings showing a whitish mass (yellow surrounded) through the dissected submucosal tunnel. Tissue samples using biopsy forceps confirmed a poorly differentiated adenocarcinoma.

cancer is difficult to diagnose prior to surgery, the presence of depressed lesions and marginal changes in the gastric folds may be indicators for diagnosis. Endoscopic characteristics of scirrhous gastric cancer involve poor distension of the gastric walls, and morphological changes in the gastric folds [11]. Morphological changes in the gastric folds of patients with LP include the presence of giant, swollen, straight, furrowed and crossed folds, resulting in a leather bottle-like appearance observed by X-ray examination. Further diagnostic indicators of LP include a waffle-like appearance detected by an upper GI endoscopic examination [12]. Although these morphological changes are important to distinguish LP from other diseases, the differential diagnosis of thickened gastric folds comprises many diseases: Menetrier's disease, hypertrophic gastritis, malignant lymphoma, rare types of aberrant pancreas, syphilis and cytomegalovirus gastritis [13]. In addition, a delayed diagnosis makes a very poor prognosis due to the aggressive nature of LP. Accordingly, it is very important to make a definite diagnosis by acquiring accurate tissue samples in clinical practice. However, in cases of malignancy, the gastric mucosa is frequently spared malignant invasion and conventional endoscopic biopsy sampling frequently fail in the accurate diagnosis [2].

Presently, several different sampling methods have been reported in a limited number of cases. In the past, the use of a diathermic snare, which permitted the acquisition of larger histological samples, referred to as endoscopic mucosal resection, was described [14]. However, this technique has a substantial risk of complications such as hemorrhage and perforation, and it is difficult to snare the non-elevated lesions associated with the solid fibrotic tissue seen in LP. Another option is to take multiple biopsies from the same site, referred to as endoscopic "forage" [15]. Unfortunately, acquiring samples blindly often provides inadequate histological material. A recent case report suggested that EUS-FNA is appropriate for the diagnosis of LP owing to its ability to sample deep submucosal lesions [16]. Although EUS-FNA, which has emerged as a standard method for sampling submucosal and pancreatic tumors, has the advantages of being rapid and convenient, appropriate tissue samples can occasionally not be acquired due to too little material and technical issues [17]. Accordingly, novel techniques with a greater diagnostic yield are required to provide proper histological tissue. We introduced a new sampling method using submucosal endoscopy which creates a short tunnel via additional submucosal dissection to access the lesion. Using this technique, we were able to visualize the tumor after tunneling into and dissecting the submucosa, allowing precise acquisition of tissue samples.

CONCLUSIONS

The present case demonstrates the benefits of our submucosal endoscopy sampling method in patients with suspected LP with malignant infiltration into the submucosa. We believe our method has significant advantages over other sampling methods.

Conflicts of interest. All authors disclose no financial relationships relevant to this publication.

Authors' contribution: T.C.: concept and manuscript writing; H.K and H.M.: critical revision of the article for important intellectual content; N.K. and R.H.: histological analysis. T.M. critical revision and final approval of the manuscript.

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