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The role of endoscopic submucosal dissection in the management of gastric inflammatory fibroid polyps: a single-center experience

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Abstract

Background and aim: Gastric inflammatory fibroid polyps constitute only 0.1% of all gastric polyps. They are usually amenable to resection by snare polypectomy. However, rarely these lesions may require resection by endoscopic submucosal dissection. This study aimed to evaluate the effectiveness and safety of endoscopic submucosal dissection in the management of gastric inflammatory fibroid polyps not amenable to resection with snare polypectomy.

Methods: A retrospective observational study of all consecutive patients who undergone endoscopic submucosal dissection for gastric inflammatory fibroid polyps between January 2011 and December 2020 was performed.

Major results: There were 9 cases of gastric inflammatory fibroid polyps resected by endoscopic submucosal dissection. Most patients were female (7/9) with mean age of 62.2 years. All gastric inflammatory fibroid polyps were described as solitary antral subepithelial lesions with mean diameter of 16.7 mm that, at endoscopic ultrasound, appeared well-circumscribed and homogeneous lesions located at *muscularis mucosa* and submucosa without deeper invasion. All lesions were successfully resected en-bloc and complete resection with free margins was obtained in 8/9 specimens. Adverse events were reported in 2/9 cases including one intra-procedural bleeding successfully controlled with hemostatic clips and one aspiration pneumonia that evolved favorably. Mean follow-up duration was 33.7 months and no delayed complications or cases of recurrence were detected.

Conclusions: Endoscopic submucosal dissection appears safe and effective for resection of gastric inflammatory fibroid polyps that present as large subepithelial lesions, if performed by experienced endoscopists after adequate characterization by endoscopic ultrasound, with high rates of technical success and low recurrence rates.

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Introduction

Inflammatory fibroid polyps (IFP), also known as Vanek tumors, are rare mesenchymal lesions of the gastrointestinal tract. They are usually solitary and may occur anywhere along gastrointestinal tract, most often in the stomach and colon. Histologically, IFP are submucosa-based but they usually extend into the mucosa and are composed of spindle cells arranged in an onion-like concentric formation around blood vessels, with prominent inflammatory cells, namely eosinophils. Other histological patterns include a short fascicular growth pattern and sparse eosinophils but prominent hyalinization. At immunohistochemical analysis, IFP typically stain for CD34 and are diffusely positive for vimentin. Their pathogenesis is thought to be related to mutations in platelet derived growth factor receptor-alpha (1).

Gastric IFP constitute only 0.1% of all gastric polyps (2). They are usually asymptomatic, although abdominal pain, gastrointestinal bleeding or intermittent gastric outlet obstruction may occur. Gastric IFP are more common in antrum and are often 2-5 cm in diameter with a smooth or slightly lobulated contour. Endoscopic ultrasound (EUS) often shows a predominantly hypoechoic mass with well-defined borders originating from the submucosal layer. They may mimic other gastric neoplasms, including adenomatous polyps, intraluminal gastrointestinal stromal tumor, carcinoid tumors or schwannomas (3). Gastric IFP are in the majority of cases amenable to resection by snare polypectomy; however, there are rare case reports of gastric IFP requiring resection by endoscopic submucosal dissection (ESD) (4-10), which are summarized in Table 1.

The aims of this retrospective study were to evaluate safety and effectiveness of ESD in the management of gastric IFP not amenable to resection with snare polypectomy due to deep subepithelial engagement on EUS and/or large size.

Methods

Patients who performed ESD for gastric IFP between January 2011 and December 2020 at the Gastroenterology Department of Centro Hospitalar e Universitário de São João (Porto, Portugal) were eligible for this study. We reviewed histopathological examination of all gastric specimens obtained from ESD procedures

performed during that period and selected those with histological diagnosis of IFP. Subsequently, the hospital electronic medical records were reviewed in order to retrieve demographic data and information related to endoscopic procedure and subsequent follow-up of all patients.

ESD procedures were performed under general anesthesia by experienced endoscopists (MM, JSA, FBS) in a standardized manner using forward-viewing endoscopy (GIF-H190; Olympus, Tokyo, Japan), after previous characterization by endoscopic ultrasound (EUS) (GFUCT140; Olympus, Tokyo, Japan) to determine the depth of invasion. A dual knife (Olympus, Tokyo, Japan) and an IT knife (Olympus, Tokyo, Japan) were used for circumferential incision and submucosal dissection, and coagulation forceps (Olympus, Tokyo, Japan) were used to achieve hemostasis during and after submucosal dissection.

All patients were admitted for post-procedure surveillance of unexpected adverse events for at least 1 day. Feeding was initiated on the second day after the procedure if patients remained stable. Initially, the patients were allowed to take a few sips of water, after which they progressively started on liquid and regular diets. Additionally, they started therapy with double-dose proton pump inhibitor for 8 weeks. All patients provided informed consent before the procedure.

Results

There were 9 cases of gastric IFP resected with ESD, which are summarized in Table 2. Most patients were female (7/9), typically presenting at 7^{th}-8^{th} decades of life with mean age at diagnosis of 62.2 years (range 44-74). Most patients (5/9) were symptomatic, and reported dyspepsia (4/9) or vomiting (1/9). In 4/9 patients, who were asymptomatic, upper digestive endoscopy had been performed for other reasons and the decision of definitive resection instead of surveillance was based on the inability to safely discard the malignant potential of the lesions and individual patient preference.

Endoscopically, all gastric IFP were described as solitary subepithelial lesions (SEL) located in the antrum with a mean diameter of 16.7 mm (range 10-25), covered by normal mucosa (Figure 1). Mucosal biopsies of the lesions were performed in 3/9

patients and, as expected, revealed non-specific histological changes (foveolar hyperplasia, chronic active gastritis) consistent with its subepithelial nature. The presence of *Helicobacter pylori* infection was tested in every patient and detected in just one in whom it was successfully eradicated. All lesions were additionally characterized by EUS, where they were uniformly described as well-circumscribed, homogeneous lesions located at *muscularis mucosae* and submucosa without invasion of *muscularis propria* (Figure 2).

All lesions were successfully resected en-bloc by ESD (Figure 3) and complete resection with free margins (R0) was obtained in 8/9 specimens. Only one resected specimen had positive deep margins. The mean diameter of resected specimens and lesions were 20 mm (range 13-32) and 12 mm (range 8-20), respectively. Additional histological changes involving the surrounding gastric mucosa included intestinal metaplasia (5/9), chronic active gastritis (2/9) and chronic atrophic gastritis (2/9).

Mean duration of procedures was 42.3 minutes (range 18-70). In 5/9 patients the ESD was performed only with dual-knife, in 1/9 patients only with IT knife and in 3/9 patients with a combination of both. Adverse events were reported in 2/9 cases including one case of intra-procedural bleeding successfully controlled with hemostatic clips and one case of aspiration pneumonia that evolved favorably with antibiotics.

Mean duration of hospitalization for post-procedure surveillance was 1.89 days (range 1-8) and during this period only one adverse event (aspiration pneumonia) was detected that required that the patient remained in the hospital for more than 2 days. Mean follow-up duration was 33.7 months (range 3-120) and every patient performed endoscopic control during this period. No delayed complications or cases of recurrence were detected in any patient during follow-up.

Discussion

Gastric IFP are usually identified incidentally as firm, solitary, sessile or pedunculated lesions, covered with a smooth surface of normal mucosa, and located in the antrum or pre-pyloric region (11). Occasionally, they may have atypical endoscopic appearances and mimic other lesions including gastric malignancy (12, 13) or a gastrointestinal stromal tumor (14). On EUS, their characteristic features include

indistinct margin, hypoechogenicity, homogeneous appearance and location within the second and/or third layer and these characteristics demonstrate close correlation with histology (15). They are most commonly asymptomatic or mildly symptomatic benign lesions, although severe complications including gastric outlet obstruction caused by ball-valve like syndrome (16,17) or massive gastrointestinal bleeding (18, 19) have been rarely reported, which underlines the importance of an adequate management and resection strategy. Interestingly, there is some evidence that *H. pylori* may play an important role in the pathophysiology of gastric IFP (20) and that they may regress with *H. pylori* eradication (21).

The management of gastric SEL is currently mainly based on EUS evaluation. For lesions < 20 mm, regular surveillance by EUS may be sufficient. Endoscopic resection may be indicated when lesions grow in size, if they measure more than 20 mm or if the diagnosis is uncertain. However, SEL characteristics on EUS may not enable diagnosis or discard malignant potential. Conventional biopsy, EUS-guided fine needle aspiration and EUS-guided fine needle biopsy all have a low diagnostic accuracy. Therefore, the current standard strategies of surveillance or definitive resection are debatable. A retrospective study demonstrated that endoscopic resection is safe and should be the procedure of choice for both diagnosis and definitive resection of gastric SEL of size under 20 mm. Regarding technical aspects and quality of resection, ESD seems superior to endoscopic mucosal resection and hybrid resection. Previous EUS is still mandatory to determine subepithelial localization and feasibility of resection as endoscopic resection is more difficult for lesions in the fourth EUS layer, with additional potential complications such as perforation and peritoneal seeding of tumor cells in case of malignant lesions (22).

The best technique for endoscopic resection of gastric IFP remains controversial. Some authors suggest that removal of gastric IFP may not be mandatory in asymptomatic patients considering that these lesions tend to maintain relatively stable over time (23). However, although rare, they have invasive potential and should be considered neoplastic rather than reactive lesions, which advises for endoscopic resection whenever possible (24). In most cases, gastric IFP are amenable to resection by snare polypectomy. Nevertheless, in rare instances, because of large size and/or

deep subepithelial engagement other techniques are required including surgical resection or ESD, as demonstrated in a retrospective study that included 54 gastric IFP, where most polyps were removed by snare polypectomy (85%), but a small proportion required resection by ESD (7%) or surgery (6%) (25). Since then, seven more cases of gastric IFP resected by ESD were reported (4-10), suggesting that this technique may play an important role in the endoscopic treatment of gastric IFP. However, large studies evaluating its safety and effectiveness for this particular indication are lacking.

To the best of our knowledge this is the largest series of gastric IFP resected by ESD described in the literature. En-bloc resection was obtained in all procedures with a high rate of complete resection with free margins. Although adverse events were reported in 2/9 cases, both were treated conservatively and only one (aspiration pneumonia) resulted in prolonged hospital admission. No cases of recurrence were detected in any patient during follow-up. Therefore, our study suggests that ESD is safe and effective for resection of gastric IFP with a high rate of complete resection, low recurrence rate and low incidence of severe adverse events.

The rare cases of gastric IFP resected by ESD reported in the literature, among which no adverse events or cases of recurrence were detected and an elevated rate of complete resection (6/7) was seen (4-10), support our findings. Of note, even in one patient with positive deep margins, there was no recurrence after 1-year follow-up (7). This technique can therefore be preferable for cases of gastric SEL with endoscopic and ultrasonographic findings suggestive of IFP where, because of submucosal invasion or larger size, snare polypectomy could be associated with increased risk of perforation or incomplete resection. In these cases, ESD could be a better option because en-bloc resection decreases the risk of retaining residual lesion at a submucosal level and avoids the danger of perforation associated with electrocautery of large-base polyps.

It is also important to define which subgroups of patients with gastric IFP could benefit more from ESD. For example, the possible influence of size in the approach is reflected in our series where most polyps were smaller than 20 mm and, among the 2/9 larger than 20 mm, one did not achieve an R0 resection. However, even this patient remains free of recurrence after a long follow-up (120 months) with several endoscopic controls since then. Therefore, our series suggests that ESD may be safe

and effective even in those polyps with more than 20 mm in size. Larger IFP are not common, but one can expect that ESD would continue to be safe and effective, namely in centers with expertise on this technique and considering alternative treatments such as surgery whenever necessary. More studies are needed to establish clear statements about the effectiveness and safety of ESD in the endoscopic management of gastric IFP in order to better define the specific role for this technique.

Our study has some limitations. First, it was a retrospective study with a small sample size. Second, follow-up duration was short in some cases and therefore our observation concerning cases of recurrence must be interpreted with caution. Despite its limitations, this is to our knowledge the largest series of gastric IFP resected by ESD to date and we provide valuable data that should be confirmed in larger multi-center prospective studies.

In conclusion, although most gastric IFP are amenable to resection by snare polypectomy with low rates of recurrence and favorable prognosis if <20 mm, in rare cases they present as SEL with features that require deeper resection by ESD in order to decrease chances of incomplete resection and avoid morbidity associated with gastric surgery. ESD appears to be a safe and effective approach for resection of gastric IFP that present as large SEL, if performed by experienced endoscopists after adequate characterization by EUS, with high rates of technical success and low recurrence rates.

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Tables

	Gender	Age (years)	Symptoms	Size (mm)	Location	Other lesions/HP	EUS findings	ESD knife	En-bloc resection	R0	Duration (min)	Adverse events	Follow-up (months)	Recurrence
(4)	Male	61	No	20	Antrum	-/+	Hypoechogenic, involving mucosa and submucosa	IT	Yes	Yes	N/A	No	29	No
(5)	Male	64	No	25	Antrum	-/-	Homogeneous, hypoechogenic, extending to deep mucosa	N/A	Yes	Yes	N/A	No	N/A	N/A
(6)	Female	61	No	10	Antrum	-/-	Homogeneous, hypoechogenic, involving mucosa and submucosa	N/A	Yes	Yes	N/A	No	N/A	N/A
(7)	Female	60	No	40	Antrum	-/-	N/A	N/A	Yes	No	N/A	No	12	No
(8)	Female	37	Abdominal pain,anemia	20	Body	-/-	Homogeneous, hypoechogenic, involving mucosa and submucosa	Dual + IT	Yes	Yes	N/A	No	24	No
(9)	Female	46	Abdominal pain	13	Antrum	-/-	Slightly heterogeneous, hypoechogenic, involving mucosa and submucosa	N/A	Yes	Yes	N/A	No	12	No
(10)	Male	73	Abdominal pain	30	Antrum	-/-	Hypoechoic, arising from muscularis mucosa	N/A	Yes	Yes	N/A	No	N/A	N/A

Table 1. Summary of cases of gastric inflammatory fibroid polyps resected by endoscopic submucosal dissection reported in the literature.

	Gender	Age (years)	Symptoms	Size (mm)	Location	Other lesions/HP	EUS findings	ESD knife	En-bloc resection	R0	Duration (min)	Adverse events	Follow-up (months)	Recurrence
#1	Female	71	Dyspepsia	25	Antrum	-/-	Well-defined, homogeneous, hypoechogenic, involving mucosa and submucosa	Dual + IT	Yes	No	60	No	120	No
#2	Female	74	No	18	Antrum	Hyperplastic polyp/-	-	Dual	Yes	Yes	70	No	19	No
#3	Male	49	Dyspepsia	12	Antrum	-/+	Well-defined, homogeneous, hypoechogenic, adjacent to muscularis mucosae	Dual + IT	Yes	Yes	20	No	3	No
#4	Female	65	Dyspepsia	15	Antrum	-/-	Well-defined, homogenous, mildly hypoechogenic, located at muscularis mucosae	Dual	Yes	Yes	18	No	50	No
#5	Male	69	No	20	Antrum	-/-	Not well defined, hypoechogenic, involving mucosa and submucosa	Dual + IT	Yes	Yes	28	No	26	No
#6	Female	60	Vomiting	15	Antrum	-/-	Well-defined, hypoechogenic, involving mucosa and submucosa	IT	Yes	Yes	45	No	62	No
#7	Female	63	No	10	Antrum	-/-	Well-defined, heterogeneous, hypoechogenic, involving mucosa and submucosa	Dual	Yes	Yes	20	Bleeding	3	No
#8	Female	65	No	10	Antrum	-/-	Well-defined, homogeneous, hypoechogenic, extending to deep mucosa	Dual	Yes	Yes	60	Aspiration pneumonia	8	No
#9	Female	44	Dyspepsia	25	Antrum	-/-	Well-defined, hypoechogenic, invading muscularis mucosae	Dual	Yes	Yes	60	No	15	No

Table 2. Summary of cases of gastric inflammatory fibroid polyps resected by endoscopic submucosal dissection at Centro Hospitalar e Universitário de São João between 2011 and 2020 (HP – Helicobacter pylori; EUS – endoscopic ultrasound; ESD – endoscopic submucosal dissection).

Figure Legends

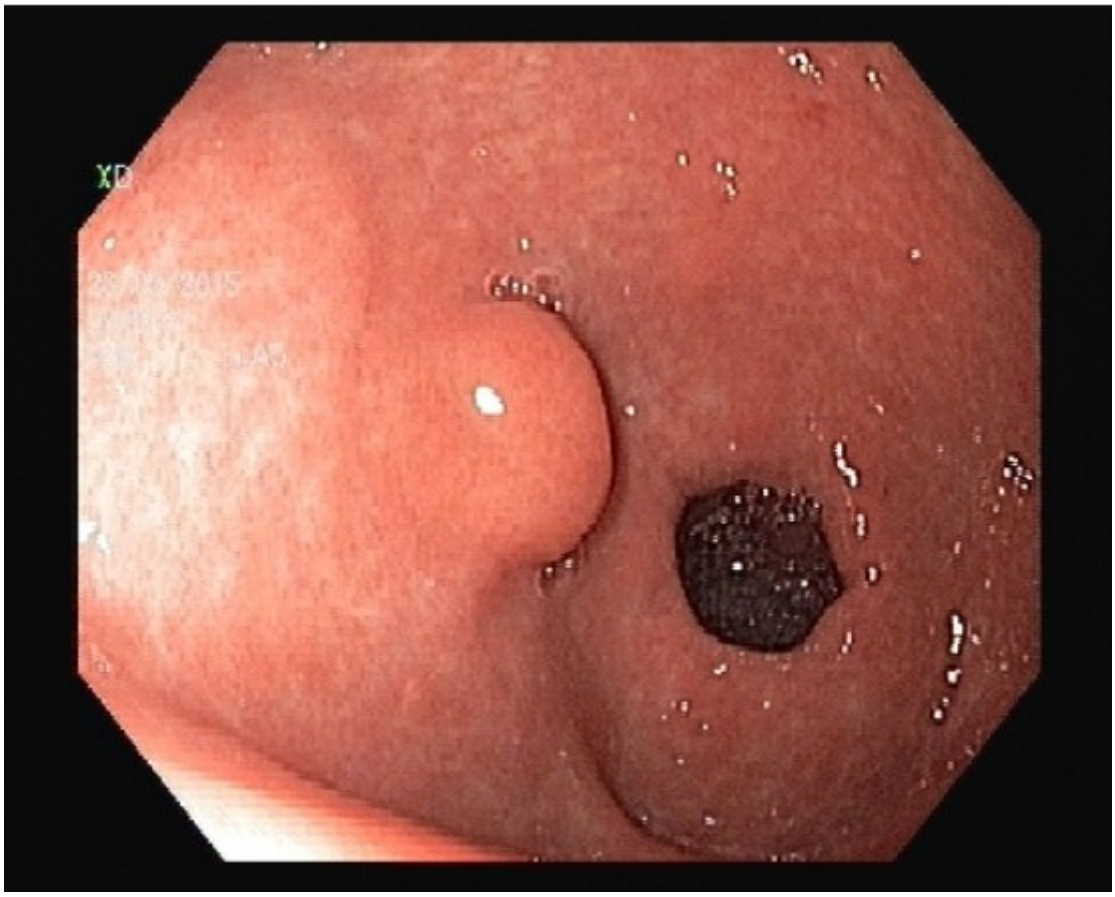

Figure 1. Upper digestive endoscopy of a 60-year-old female patient. A gastric inflammatory fibroid polyp is seen as an antral subepithelial lesion with 15 mm diameter.

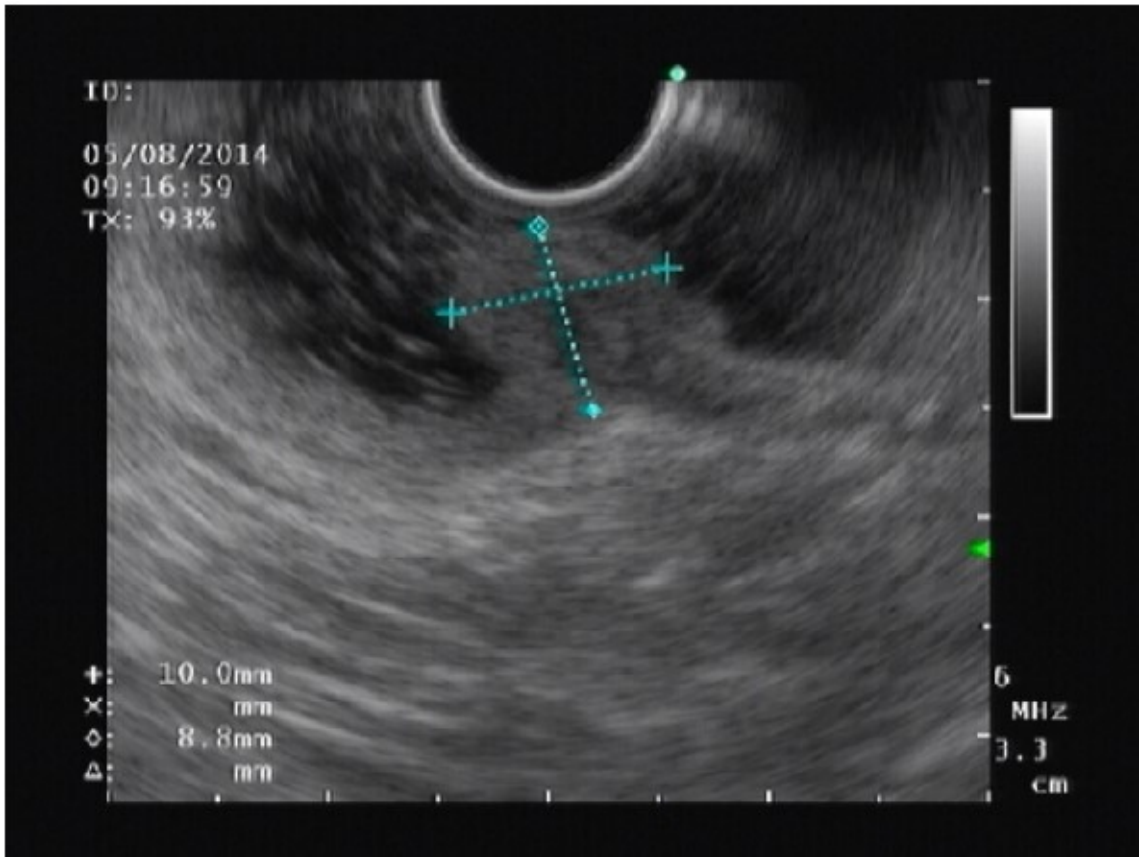

Figure 2. Endoscopic ultrasound performed at the same patient described in Figure 1. The lesions is as an homogeneous, hypoechogenic, round, mildly heterogeneous lesion with well-defined contour, measuring 10x9 mm, located at deep mucosa and submucosa.

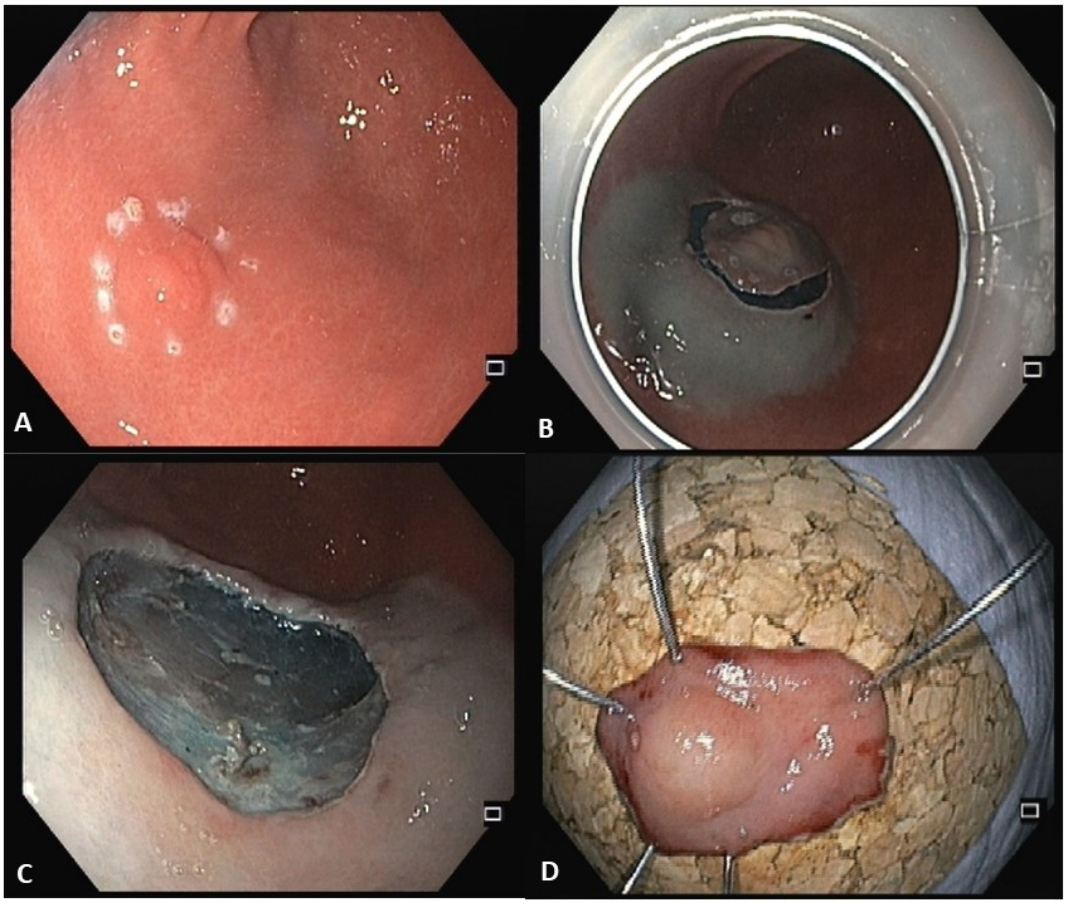

Figure 3. Endoscopic submucosal dissection of a gastric inflammatory fibroid polyp with 10 mm diameter in the anterior surface of the antrum. A. First, the limits of the planned resection margin were marked with the dual-knife. B. Submucosal injection and incision around the lesion respecting the margins previously defined. C. Scar at the end of the procedure after complete resection of the lesion. D. Resected specimen adequately mounted and fixated in a cork plaque.