

Endoscopic diagnosis and treatment of calcifying fibrous tumors

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ABSTRACT

Background/Aims: The calcifying fibrous tumor (CFT) is classified as a benign fibrous lesion, and it is a rare pathologic entity. We evaluated the feasibility, efficacy and safety of endoscopy treatment for CFT.

Materials and Methods: We retrospectively analyzed a total of 4 gastric CFTs that were treated with ESD or EFR at the endoscopic center of Zhongshan Hospital, Fudan University, in Shanghai, between Jan 2007 and Sept 2011. We used endoscopic ultrasound (EUS) to assess whether endoscopy treatment was suitable. Tumor characteristics, complications, the en bloc resection rate, and the local recurrence rate were evaluated.

Results: Of the 4 patients, the median age was 55.5 years old. The mean maximum size of the lesions was 1.95 ± 0.67 (range: 1.0-2.5). The EUS features of the lesions included a mass in the muscularis propria of the gastric wall and a heterogeneous hypoechoic (1/4) or homogeneous (3/4) hypoechoic pattern. All of the endoscopic treatments were completed successfully. The en bloc resection rate was 100%. Confirmed diagnoses were made by pathologic results. No local recurrence or complications were observed during the follow-up period (ranging from 15 to 28 months).

Conclusion: Endoscopic treatment, especially ESD/EFR, appears to be a feasible and safe procedure for CFT with relatively few complications and low mortality.

Keywords: Endoscopic submucosal dissection, submucosal tumor, calcifying fibrous tumor

INTRODUCTION

The calcifying fibrous tumor (CFT) is classified as a benign fibrous lesion, and it is a rare pathologic entity. It was first described by Rosenthal et al. (1) in 1988 as a "childhood fibrous tumor with psammoma bodies" in two children presenting with lesions in the extremities. Fetsch et al. (2) subsequently reported on 10 similar tumors in varying locations in individuals ranging from 1 to 33 years of age, and they were the first to use the term "calcifying fibrous pseudotumor" (CFP). This condition has recently been renamed "calcifying fibrous tumor (CFT)" because of its small but significant tendency to recur locally (3). A review of the literature reveals that CFTs usually occur in the soft tissue of the extremities, trunk, axilla, pleura, mediastinum and peritoneum; CFTs of the gastrointestinal tract are quite rare (4). In this study, we analyzed the clinicopathology of 4

gastric CFTs, for the first time, introduced endoscopic treatment for CFTs.

MATERIALS AND METHODS

We retrospectively analyzed our database of all patients who underwent endoscopic treatment at the endoscopic center of Zhongshan Hospital, Fudan University, in Shanghai, between Jan 2007 and Sept 2011. Four patients with gastrointestinal submucosal tumors (SMTs) were histologically diagnosed with CFTs by pathologists. Endoscopic ultrasonography (EUS) was performed before treatment with a UM-2000 system (Olympus, Tokyo, Japan) for all the 4 patients, evaluating the origin and size of the tumors, which helped us to choose a suitable endoscopic treatment method or if the endoscopic-laparoscopic surgery was chosen. Informed consent for all procedures, including endo-

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scopic resection, was obtained from each patient. We obtained the institutional review board (IRB) approval for the study.

Equipments

Standard single-accessory-channel endoscopy (GIT-H260; Olympus, Tokyo, Japan and AQ100, Aohua, Shanghai, China) or dual-channel endoscopy (GIF-2T240; Olympus, Tokyo, Japan) was used during the procedures. A transparent cap (ND-201-11802; Olympus, Tokyo, Japan) was attached to the front of the endoscope. An IT knife (KD-611; Olympus, Tokyo, Japan) and a hook knife (KD-620LR; Olympus, Tokyo, Japan) were used to dissect the submucosal layer and to peel the tumor. The high-frequency generator used was the HybridKnife system (ERBE, Tuebingen, Germany). Other equipment included injection needles (NM-4L-1; Olympus, Tokyo, Japan), grasping forceps (FG-8U-1; Olympus, Tokyo, Japan), snares (SD-230U-20; Olympus, Tokyo, Japan), hot biopsy forceps (FD-410LR; Olympus, Tokyo, Japan), clips (HX-600-135; Olympus, Tokyo, Japan) and endoloops (MAJ-339; Olympus, Tokyo, Japan).

Endoscopic treatment

Endoscopic treatment was performed as shown in Figure 1. Several marker dots were made approximately along the margin of the lesion with argon plasma coagulation (APC) for tumor location. After injection of several milliliters of submucosal injection solution (100 mL saline +5 mL 0.2% indigo carmine + 1 mg epinephrine) into the submucosal layer, the mucosa was incised outside the marker dots with the IT or hook knife. The submucosal tissue was then gradually dissected to expose the tumor in the muscularis propria. The solution was injected repeatedly during the dissection whenever necessary. The hook knife was used to carefully dissect the lesion along the margin of tumor. This endoscopic operation was

called endoscopic submucosal dissection (ESD). If the tumor can not be separated from serosa, we used IT knife to resect the whole tumor along with the serosa, paying no attention to the defection of gastric walls. The principle was to resect the tumor without residual. Exposed vessels on the artificial ulcer were coagulated with APC or hot biopsy forceps to prevent delayed bleeding, and metallic clips and endoloops were always used to close the wounds. This endoscopic technique was named endoscopic full-thickness resection (EFR) (Figure 2) (5,6).

Pathologic evaluation and follow up

A resection without interruption of the tumor capsule and with a tumor-free margin, in which both the lateral and basal margins were free of tumor cells, was considered a complete resection (CR). Immunohistochemical staining on the organization with antibodies S-100, smooth muscle antigen, vimentin, desmin, CD117, and CD34 was done. Histopathologic evaluations were performed by a pathologist.

The patients were followed up with endoscopy at 2, 6, and 12 months after the last endoscopic resection and then annually thereafter. EUS was performed when there seemed to be a residual or recurrent lesion at the resection site.

RESULTS

There were 2 men and 2 women patients, with the median age of 55.5 (range: 46-63) years. The mean maximum tumor size was 1.95 ± 0.67 (range: 1.0-2.5) cm. All the patients had symptoms, although most of them felt abdominal discomfort and not specific symptoms. When we told the patients of their condition and the possible treatment choices, they chose endoscopic treatment.

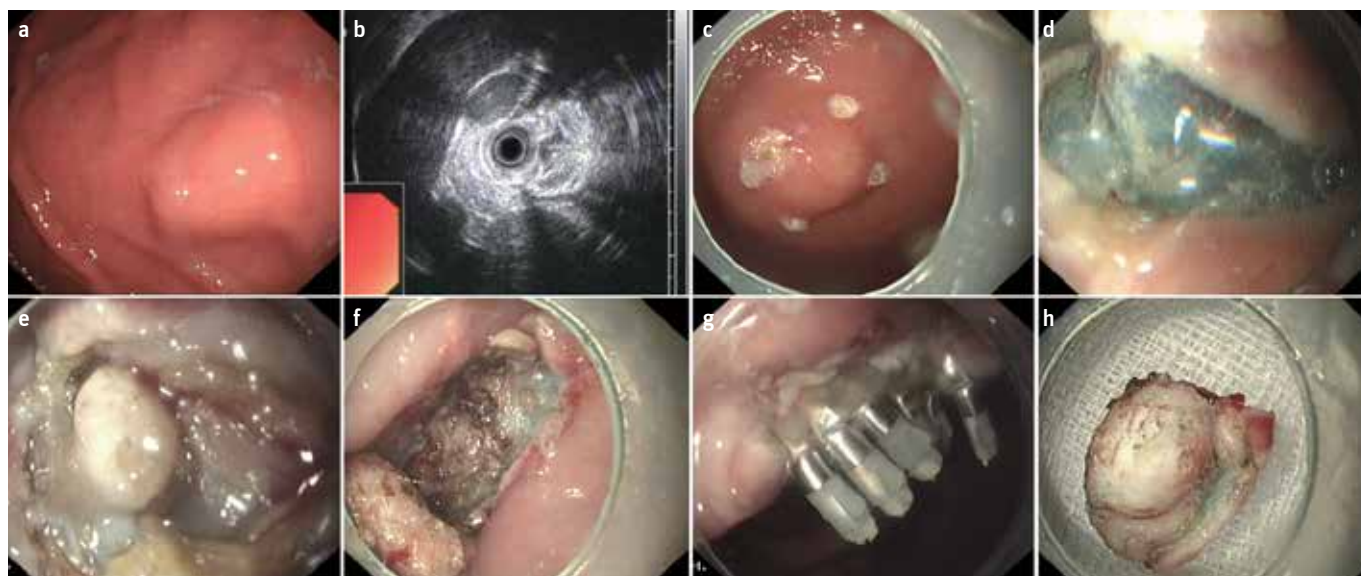


Figure 1. ESD to Treat Calcifying Fibrous Tumors

(a-b) Images from endoscopy and endoscopic ultrasonography of gastric CFTs. (c) Marker dots being made near the lesion. (d) After injection of solution around the lesion to lift the mucosal layer, the mucosa was then incised outside the marker dots. (e) The hook knife was used to carefully dissect the lesion along the margin of tumor. (f) The wound after stripping. (g) Clip the wound. (h) The tumor.

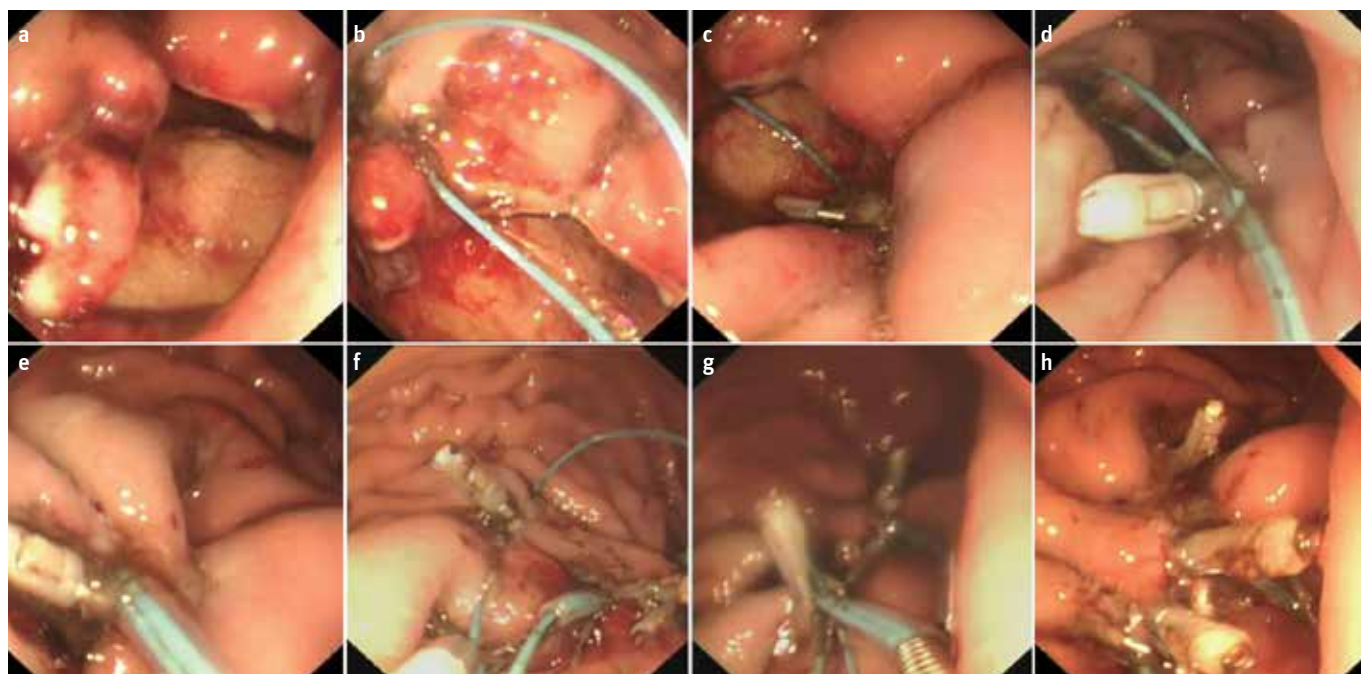


Figure 2. Close the gastric wall defect after EFR with metallic clips and endoloops.

(a)The gastric wall defect after ESD. (b-c) The endoloop was fixed to the both side of the gastric wall defect using two metal clips. (d-e)Close the defect by tightening up the endoloop. (f-g) Repeat the step B to step E. (h) The gastric wound was closed with several metallic clips and endoloop successfully.

Table 1. Clinicopathologic Features and Endoscopic Treatment of Calcifying Fibrous Tumors From This Study (n = 4)

No.	Sex	Age (year)	Chief complaint	Site	Size (cm)	Layer	Echo	Growth	Treatment	Perforation (active)	Hospital stay-in (day)	follow-up time (month)	Complication
Case 1	Female	58	Abdominal discomfort	Gastric body	2.3	Muscularis propria	Heterogeneous hypoechoic	Extraluminal growth	ESD	No	2	15	No
Case 2	Female	46	Abdominal discomfort	Gastric body	1	Muscularis propria	Homogeneous hypoechoic	Intraluminal growth	ESD	No	2	26	No
Case 3	Male	63	Abdominal discomfort	Gastric body	2	Muscularis propria	Homogeneous hypoechoic	Extraluminal growth	EFR	Yes	5	28	No
Case 4	Male	53	Abdominal discomfort	Gastric antrum	2.5	Muscularis propria	Homogeneous hypoechoic	Extraluminal growth	EFR	Yes	3	16	No

Calcifying fibrous tumors, as viewed by endoscopy in our study, appeared as well-circumscribed SMTs with normal overlying mucosae. The EUS features of the lesions included a mass in the muscularis propria of the gastric wall and a heterogeneous hypoechoic (1/4) or homogeneous (3/4) hypoechoic pattern. Patient characteristics, lesion features and clinical outcomes are summarized in Table 1. All of the endoscopic treatments were completed successfully. Control of bleeding with APC, hot biopsy forceps and/or hemoclips was successful during the operations. The tumors and serosae were resected simultaneously to achieve complete resection (CR percentage 100%), and the wounds, no matter they were done on ESD (2/4) or EFR (2/4), were successfully managed with hemoclips without laparoscopic assistance. No serious complications occurred during or after treatment. All of the patients were hospitalized for observation; the median hospital stay was 2.5 (2-5) days. Confirmed diagnoses were made by pathologic results. The

median duration of follow-up was 21 months (ranging from 15 to 28 months). No local recurrence or complications were observed during the follow-up period.

DISCUSSION

CFTs present as painless, benign, soft-tissue or subserosal lesions with wide anatomical distribution, commonly in children, adolescents and young adults, with no obvious sex bias (3). With no special symptoms and no specific endoscopic/EUS findings, it is difficult to differentiate CFTs of the gastrointestinal tract from other gastrointestinal SMTs, such as gastrointestinal stromal tumors (GISTs), heterotopic pancreas (HP), carcinoid tumors, lipomas, inflammatory myofibroblastic tumors, and reactive nodular fibrous tumors. Histologically, CFTs are characterized by a proliferation of bland (myo)fibroblastic spindle cells embedded in a dense, hyalinized stroma, showing variable degrees of mineralization and inflammation(3). Immunohistochemical

studies demonstrate that the lesional cells are immunoreactive for vimentin, variably immunoreactive for musclespecific actin, smooth muscle actin, desmin, and CD34. However, the stain for anaplastic lymphoma kinase (ALK) is negative (7)

Many professionals have suggested that asymptomatic gastrointestinal submucosal tumors (< 3 cm) could be followed-up with periodic endoscopy. However, this approach must take into account patient compliance, cost-effectiveness, the risk associated with repeated endoscopic procedures, and delayed diagnosis of malignancy. CFT recurrence following excision has been reported, and this recurrence had the same morphology as the primary lesion (8). However, recurrence occurs primarily when the initial resection is incomplete, and malignant transformation has not been reported, so simple, local excision is still the preferred therapeutic approach in treating CFTs. Although convenient, when using conventional surgery or laparoscopic surgery, it is sometimes difficult to identify a precise resection area without the assistance of an endoscopy. Furthermore, when excising larger areas, operative complications, such as indigestion, obstruction and adhesion, can easily occur.

ESD was initially developed in Japan for the resection of early gastric cancer. ESD not only offers the promise of localized treatment but also makes it possible to resect whole lesions and provide precise histological information. With the enrichment of experience in ESD, endoscopic submucosal excavation and EFR were developed from ESD in order to remove submucosal gastrointestinal lesions, such as those that reach the muscularis propria layer and/or have close proximity to the serosa. EFR has produced good therapeutic effects and reduced the normal tissue resection(6). All four CFTs in this study originated from the muscularis propria, and 3 of 4 cases were extraluminal-growing. Perforation is likely to occur during endoscopic resection of this kind of lesion. For gastric lesions, we could repair the perforation using metallic clips with or without endoloops.

In conclusion, CFTs are difficult to diagnose when relying only on features derived from gastroscopy and EUS. Endoscopic

treatment, especially ESD/EFR, appears to be a feasible and safe procedure for not only diagnosis but also treatment. However, more experiences are needed to confirm our results.

Conflict of Interest: No conflict of interest was declared by the authors.

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