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Gastric calcifying fibrous tumors

Computed tomography findings and clinical manifestations

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Abstract

To retrospectively analyze the computed tomography (CT) findings and clinical manifestations of gastric calcifying fibrous tumor (CFTs).

The features of 7 cases with pathologically proven gastric CFTs who had undergone CT were assessed, including tumor location, contour, growth, degree of enhancement, calcification and clinical data. In addition, the size and CT value of each lesion were measured. The mean values of these CT findings and clinical data were statistically analyzed only for continuous variables.

Four patients were female and three were male (mean age: 33.3 years; range: 22 ~ 47 years). Nonspecific clinical symptoms: abdominal pain and discomfort were observed in four cases and the CFTs were incidentally detected in the other three cases. Regarding tumor markers, lower ferritin levels were observed in three female patients. All of the gastric CFTs were solitary and mainly located inside the body; they were in round or oval shape and exhibited endophytic growth. Gastric CFTs are usually small sized and could contain confluent and coarse calcifications; cyst, necrosis, ulcer, bleeding and surrounding lymphadenopathy were not found in any of the cases. Unenhanced CT values of gastric CFTs were higher than those of same-transect soft tissue. Mild-to-moderate enhancement in the arterial phase and progressive enhancement in the portal venous phase were mainly noted.

A gastric mass with a high unenhanced CT attenuation value, confluent and coarse calcifications and mild-to-moderate enhancement could prompt a diagnosis of gastric CFT. In addition, (1) being young- or middle-aged, (2) having relatively low ferritin levels, and (3) tumor located in the gastric body have critical reference value for diagnosis of gastric CFT.

Abbreviations: CFT = calcifying fibrous tumor, CT = computed tomography, DE = degree of enhancement, DEAP = degree of enhancement in the arterial phase, DEPP = degree of enhancement in the portal venous phase, ESD = endoscopic submucosal dissection, ESE = endoscopic submucosal excavation, GST = gastric stromal tumor, HU = Hounsfield unit, LAD = long axis diameter, ROI = region of interest, SAD = short axis diameter.

Keywords: calcifying fibrous tumor, gastric neoplasm, subepithelial tumors, X-Ray computed tomography

1. Introduction

Calcifying fibrous tumor (CFT), a rare benign mesenchymal tumor, is rarely prone to multiply and has a slightly higher female preference (57.3%). A CFT can occur anywhere in the body but is most commonly found in the stomach (18.6%) or small intestine (13.6%), followed by the pleura (9.5%), neck (5.5%) and colon and rectum (5.5%), however, reports in the other locations are sporadic.[1–14] Most gastric CFTs originate from submucosa in

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The authors declared that there is no conflict of interest. Each author has participated sufficiently in this research.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Consent to publication was obtained from all individual participants included in the study.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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the stomach, followed by muscularis propria and subserosa. Except for their small size and easy calcification, CFTs have no specific X-ray computed tomography (CT) or clinical characteristics.[1,7–12] Although CFTs are primarily found in the stomach, accurate preoperative diagnosis is extremely difficult due to their low incidence, and these tumors can easily be misdiagnosed as other mesenchymal tumors, such as gastric stromal tumors (GSTs), schwannoma, and leiomyoma.

Misdiagnosis of gastric CFTs is related to their rarity; also, images of CFTs appear similar to those of other mesenchymal tumors, particularly GSTs. As potentially malignant tumors, GSTs have high recurrence and metastasis rates even when small, and surgical treatment is preferred if a GST is suspected.[15] By contrast, gastric CFTs are benign tumors exhibiting slow growth. Because patients with CFTs get nonspecific symptoms, they are usually detected incidentally. If a preoperative diagnosis of gastric CFT is clearly accurate, surgery may be avoided or at least be optimized. Therefore, accurate preoperative gastric CFT diagnosis is of high clinical value.

As far as we know, there have been no reports on CT features with large samples or systematic analysis of gastric CFT, and only sporadic cases have been reported. In clinical practice, CT imaging plays a subsidiary role for diagnosis and preoperative evaluation of gastric diseases; therefore, this study focused on determining characteristic CT features and clinical manifestations of gastric CFTs to improve understanding of these tumors for clinical and imaging physicians.

2. Materials and methods

Our institutional review board approved this retrospective study and waived the requirement for informed consent from patients.

2.1. Patients

We searched the database of Tongde Hospital of Zhejiang Province and First affiliated Hospital of Bengbu Medical College from January 2007 to October 2018 and found seven patients were pathologically confirmed as having gastric CFTs (three men, four women; mean age ± standard deviation, 33.3 ± 8.90 years; age range, 22–47 years). Clinical and surgical data of these patients were summarized and reviewed (Table 1).

2.2. CT image acquisition

Unenhanced and contrast-enhanced CT scans were performed using multidetector CT (MDCT) scanners (SOMATOM Sensation 16, Siemens Healthcare, Forchheim, Germany; Siemens Definition AS 40, Siemens Healthcare; SOMATOM Definition Flash, Siemens Healthcare; LightSpeed VCT, GE Healthcare, Milwaukee, WI).

For each patient, contrast-enhanced images of the arterial phase and portal venous phase (with 30- and 60-second delays, respectively) were acquired. By using a power injector (Ulrich Medizintechnik, Buchbrunnenweg, Germany), 150 mL of contrast agent iopamidol with 300 mg/mL iodine (Iopamiro, Bracco Sine, Shanghai, China) or iohexol with 300 mg/mL iodine (Omnipaque 300, Amersham, Shanghai, China) was injected (at a rate of 3–5 mL/s) through a large-bore peripheral intravenous catheter into a medially located antecubital vein. The scanning parameters for CT examination were set as follows: for SOMATOM Sensation 16, beam collimation = 1.2 mm × 16, pitch = 1, kVp/effective mA = 120/300, and gantry rotation time = 0.5 seconds; for Siemens Definition AS 40, beam collimation = 1.2 mm × 40, pitch = 1, kVp/effective mA = 120/300, and gantry rotation time = 0.5 seconds; for SOMATOM Definition Flash, beam collimation = 1.2 mm × 32, pitch = 1, kVp/effective mA = 120/300, and gantry rotation time = 0.5 seconds; for LightSpeed VCT, beam collimation = 0.625 mm × 64, pitch = 0.984, kVp/mA = 120/100–300, and gantry rotation time = 0.6 seconds. MDCT was performed during inspiratory breath holding. The 5- or 7-mm slice thickness of the original images was reconstructed into 2-mm slice thickness and the images were uploaded to a picture archiving and communication system (PACS; GE Healthcare-Centricity RIS CE V2.0; GE Medical Systems, Fairfield, CT).

2.3. Image analysis

All CT findings were reviewed in stack mode in a PACS workstation. Two radiologists (each with 13–14 years' experience) interpreted the CT images independently and then collaborated to determine the characteristic features of gastric CFTs.

Based on unenhanced and contrast-enhanced CT images, the radiologists assessed the following CT characteristics:

(a) size,
(b) location,
(c) contour,
(d) growth pattern,
(e) presence of calcification, and
(f) degree of enhancement (DE).

Other CT findings such as intralesional necrosis, surface ulceration, hemorrhage, and lymphadenopathy were not analyzed in this study because the cases were absent of these features.

Table 1

Summary of clinical features of gastric CFTs.

Case No.	Age/Sex	Clinical manifestations/ Continue time	Ferritin lever/Ug/L	PD	Surgery	Origin	Follow-up time
1.	25/M	Abdominal discomfort/2Y	No data	GST	ESD	SM	Absent
2.	22/M	Abdominal pain/6M	55.3	GST	ESD	SM	24 month
3.	47/F	Incidental	6.60	GST	ESE	SM	10 month
4.	35/F	Abdominal pain/1M	63.6	GST	ESE	MP	Absent
5.	30/M	Incidental	99.8	GST	ESE	MP	Absent
6.	32/F	Abdominal pain/3M	8.30	GST	ESE	SM	6 month
7.	42/F	Incidental	10.16	GST	ESE	SS	Absent

ESD = endoscopic submucosal dissection, ESE = endoscopic submucosal excavation, F = female, GST = gastric stromal tumor, M = male, M = month, MP = muscularis propria, Normal serum ferritin lever = 13.00–150.00 Ug/L, PD = preoperative diagnosis, SM = submucosa, SS = subserosa, Y = year.

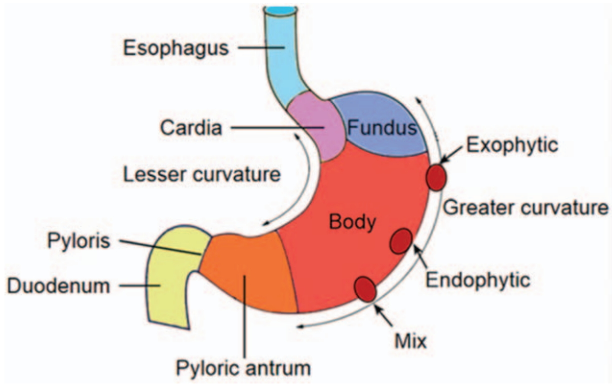

Figure 1. Flow of this study based on recommended standards for differentiating diagnosis of gastric CFTs.

The locations were classified into cardia, fundus, body, and antrum (Fig. 1), and contours were categorized as round or oval. Three growth patterns were identified: endophytic (mass completely located in the gastric lumen without bulging into the exophytic space), exophytic (tumor confined to the extraluminal space without protruding into the gastric lumen), and mixed type (mass exhibiting features of endophytic and exophytic growth; Fig. 1). Unenhanced CT attenuation values higher than 100 Hounsfield unit (HU) were considered as intralesional calcification. Degree of enhancement (DE) in the arterial phase (DEAP) and in the portal venous phase (DEPP) was respectively calculated. DE was divided into 3 types, namely mild (DE: 0–20 HU), moderate (DE: 21–40 HU), and severe (DE: >40 HU). Two radiologists measured the long (LAD) and short axis diameter (SAD) of lesions in maximal transverse images. The CT attenuation values of lesions and soft tissue (erector spinae muscle) were measured in HU by the two radiologists using 10 to 30-mm^2 circular regions of interest (ROIs) at the corresponding level in the same cross-sectional unenhanced and contrast-enhanced CT images. The DEAP and DEPP were subsequently calculated. The researchers carefully drew the ROI cursors to encompass as much of the highly enhanced lesion areas as possible and to exclude necrosis, calcification, fat, and adjacent tissues and organs. Each ROI was measured twice and then the average value was obtained.

2.4. Statistical analysis

The mean and standard deviation of quantitative data (age, size, and CT attenuation value) was assessed using SPSS 22.0 (IBM, Chicago, IL).

3. Results

3.1. Clinical features

The clinical features of gastric CFT patients are summarized in Table 1. Four patients were female and 3 were male (mean age: 33.3 years; age range: 22–47 years). The patients exhibited nonspecific clinical symptoms: abdominal pain and discomfort were observed in 4 cases and the other 3 cases were incidentally detected. Regarding tumor markers, only ferritin levels were lower in three female patients, while the other markers (CA-199, CA-125, AFP, CEA and PSA) were negative for all cases; none of the patients were further followed up for tumor markers. All cases were misdiagnosed as GSTs (including 2 cases misdiagnosed by gastroscopy) and underwent surgery, after which three cases were followed up for 6 to 24 months without abnormalities.

3.2. Qualitative analysis of CT findings

The results of salient qualitative image analysis are presented in Table 2. Five gastric CFTs were located in the body (Figs. 2 and 3), with 3 in the lesser and 2 in the greater curvature of the stomach. The lesions of the remaining 2 cases were observed in antrum and fundus of the stomach, respectively (Fig. 4). All tumors were solitary, round or oval in shape, and without evident lobulation. Endophytic growth was observed in five cases with one case contained calcification; two exophytic lesions contained calcification. Calcification refers to spots scattered in the center or at the periphery of a tumor, and the number of calcifications was more than three (Figs. 2 and 4). No signs of cysts, necrosis, ulcers, bleeding, or surrounding lymphadenopathy were identified in all of the cases. After enhancement, 6 tumors exhibited mild-to-moderate enhancement; only one severe enhancement was observed.

3.3. Quantitative analysis of CT findings

The results of qualitative CT image analysis are summarized in Table 3. CT attenuation values of 3 phases, CT attenuation values of soft tissue (erector spinae muscle), and tumor sizes were measured. Variance in tumor size was low in the tumors with LAD ranging from 1.0 to 2.9 cm (mean: 1.6 cm) and the standard deviation ranging from 0.9 to 2.7 cm (mean: 1.3 cm). All the unenhanced CT values of gastric CFTs were more than 48 HU (rage from 48.7 HU to 71.0 HU), which was similar with the same-transect soft tissue (rage from 47.8 HU to 62.5 HU). Post-enhancement CT mainly revealed mild-to-moderate enhancement in the arterial phase with CT attenuation values of 63.1–95.0 HU (mean CT value: 78.3 HU) and progressive enhancement in the

Table 2

Qualitative CT findings of gastric CFTs.

Case No.	Location	Contour	Growth pattern	Calcification	Enhancement in the AP/PP
1.	Body	Oval	Endophytic	Absent	Mild/Mild
2.	Body	Round	Endophytic	Stippled	Moderate/Moderate
3.	Antrum	Oval	Exophytic	Stippled	Mild/Moderate
4.	Body	Round	Endophytic	Absent	Mild/Mild
5.	Fundus	Oval	Endophytic	Stippled	Mild/Moderate
6.	Body	Round	Endophytic	Absent	Severe/Moderate
7.	Body	Round	Exophytic	Stippled	Mild/Mild

AP = arterial phase, PP = portal venous phase.

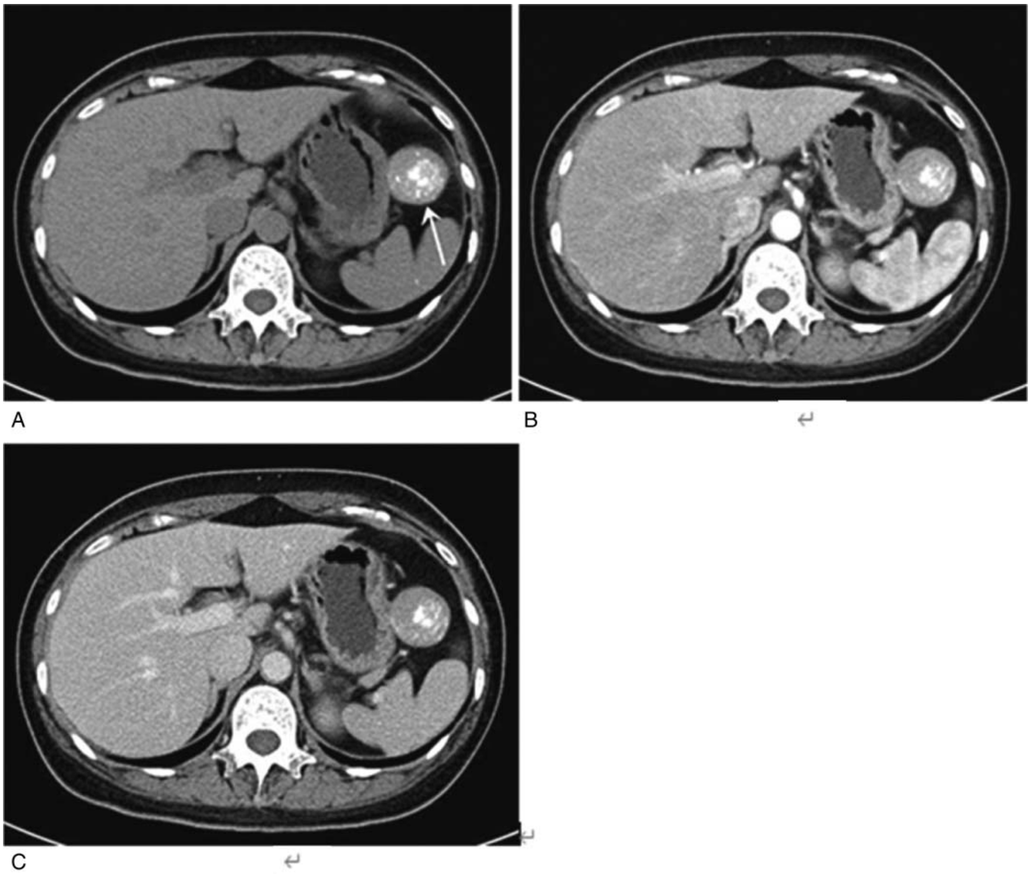

Figure 2. A 42-year-old woman with a gastric CFT. Axial (A) unenhanced CT scan depicts a round exophytic mass at greater curvature of the gastric body (↑); furthermore, confluent and coarse calcifications can be seen on the periphery and in the center of the tumor. Axial (B) contrast-enhanced CT scan shows a mildly enhanced mass in the arterial phase. Axial (C) contrast-enhanced CT scan shows a gradually enhanced mass in the portal venous phase.

portal venous phase with CT attenuation values of 67.9–99.7 HU (mean CT value: 85.5 HU). In addition, the DEs were incremental in the DEAP (mean: 18.8 HU; range: 5.4–43.0 HU) and DEPP (mean: 29.1 HU; range: 8.3–37.0 HU).

4. Discussion

CFTs were first observed by Rosenthal and Abdul-Karim in 1988,[16] but it was not until 2001 that a gastric CFT was first reported by Puccio et al.[17] Thus far, 37 cases of gastric CFTs have been reported in 23 studies in PUBMED, including some published in French or Japanese.[7–12,17–33] Gastric CFTs are rare and easily misdiagnosed as GSTs that possess malignant potential before surgery, which may lead to unnecessary surgical treatment. The purpose of this study was to improve radiologists or surgeons' clinical and image-based understanding of gastric CFTs through systematic analysis of their clinical and CT manifestations, which in turn provides opportunity to optimize treatment.

Gastric CFTs are benign tumors most commonly found in the stomach of the middle-aged individuals (mean age of occurrence: 51.4 years, age range: 25–77 years). They have a slightly higher preference for females (57.3%) and most originate in the submucosal layer (69.6%), followed by the muscularis propria (21.7%) and serous layer (8.7%).[7–12,17–33] In addition, half of the gastric CFTs in this study were detected incidentally during physical examinations for other diseases; the other half had nonspecific symptoms such as abdominal pain, distension, discomfort, nausea, and vomiting.[17,21,23–30,32] The clinical data of the patients in the present study were similar to those in previous studies,[3–9] except that the patients were younger (mean: 33.3 years). Notably, abnormally low ferritin levels were observed in three female patients among 6 tumor markers. Whether lower ferritin is helpful for differential diagnosis of gastric CFTs from GSTs requires further investigation.

Gastric CFTs are mainly located in the body with no evident variation in lesser or greater curvature, and are round or oval in shape with calcification.[8–11,17,19–20,22–31,33] The regular shape may be related to the small size and benign biological behaviors of CFTs. As a form of noninvasive examination, CT has many irreplaceable advantages for evaluation of gastric neoplasms: it can not only clearly display lesion locations but also accurately evaluate the relationships between lesions and the stomach/surrounding tissues or organs. To our knowledge, there were only six reports on CT images of CFTs, all of which were case reports.[8–10,24,27,31] Of these reports, only 2 cases have demonstrated mild-to-moderate delayed enhancement, and three have revealed confluent and coarse calcifications at peripheral areas and centers of tumors; however, enhancement and calcification have not been mentioned in most reports. In our study, the characteristics of enhancement and calcification were very similar to those in two other studies.[9,24] In previous studies,

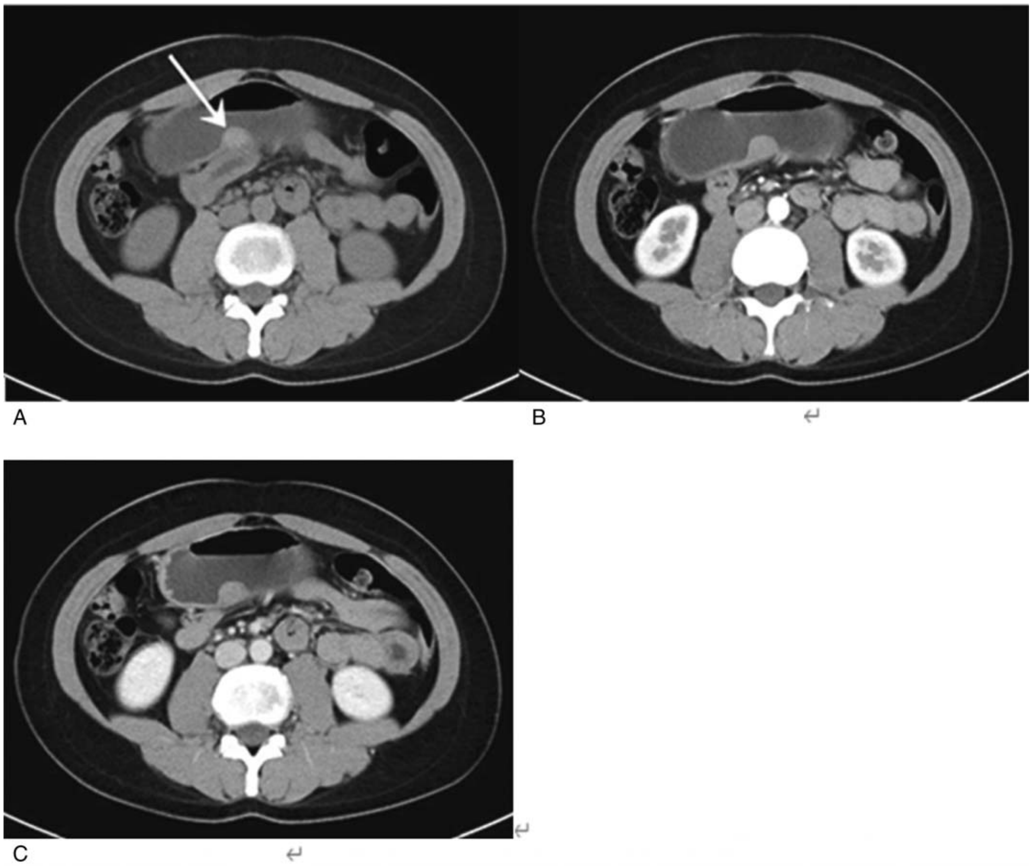

Figure 3. A 35-year-old woman with a gastric CFT. Axial (A) unenhanced CT scan exhibits an oval endophytic mass at greater curvature of the gastric body without calcification (↑). Axial (B) contrast-enhanced CT scan shows a mildly enhanced mass in the arterial phase. Axial (C) contrast-enhanced CT scan shows a moderately enhanced mass in the portal venous phase.

pre- and post-enhancement CT features were primarily determined based on ratios of spindle cells, collagen, calcification, fibrous components, and lymphoplasmacytic inflammatory infiltrates in gastric CFTs.[3,7–9,10,24]

Through comprehensive analysis of previous studies, we found that three imaging findings, namely small size (mean: 2.1 cm), a high unenhanced CT attenuation value (mean: 51.9 HU), and moderate enhancement (mean: 23.1 HU), should facilitate diagnosis of gastric CFTs.[7–12,18–32] Most related reports have mentioned tumor size but overlooked CT attenuation value, which has been carefully evaluated in only 2 studies.[3,24] The results were very similar to the only two above-mentioned CT report, which may be due to benign biological behavior, poor blood supply, slow growth, or abundant calcification and fibrosis in tumors.[9,24] In addition, it was as expected that the unenhanced CT attenuation value of gastric CFTs was similar to the same cross-sectional erector spinae muscle by measure. Furthermore, the DEAP was mild, the DEPP was moderate, and all CT attenuation values of the two phases were between 60 and 100 HU. We focused on these quantitative indices to acquire a more objective, comprehensive, and accurate understanding of the CT features of gastric CFTs. It is worth mentioning that gastric schwannomas and CFTs share many similar CT characteristics: more common in the gastric body, endophytic growth and progressive enhancement, but rare calcification was detected in the former.[34] It is difficult to distinguish CFTs from gastric leiomyoma and gastric polyp, as well as GSTs and gastric schwannomas because of their similar CT findings, even by experienced radiologists or clinicians. But gastric leiomyoma shows some specific characteristics including the good hair at cardia, homogeneous density, mild to moderate enhancement, uncommon cystic degeneration and calcification; gastric polyps often occur in the submucosa of gastric antrum, featured by intraluminal growth, pedicle, obvious enhancement and rare calcification.[35–36]

Benign gastric CFTs are easily misdiagnosed as GSTs—the most common and potentially malignant type of mesenchymal tumor. However, GSTs are usually large and prone to cystic degeneration, necrosis, and rare calcification. In addition, most GSTs exhibit moderate to severe heterogeneous enhancement in contrast-enhanced CT images.[37–38] For examination of gastric CFTs, both gastroscopy and fine needle aspiration biopsy were traumatic and difficult to reach definitive diagnosis.[9–11] However, distinguishing between the 2 types of tumor through noninvasive CT examination before surgery is of high clinical value, and could assist doctors in selecting reasonable and effective treatments for patients.

In this study, the CT features of gastric CFTs were deeply analyzed in combination with previous literatures. We recommend that patients should undergo endoscopic submucosal dissection (ESD) surgery or be followed up if gastric CFTs are highly suspected on CT findings.

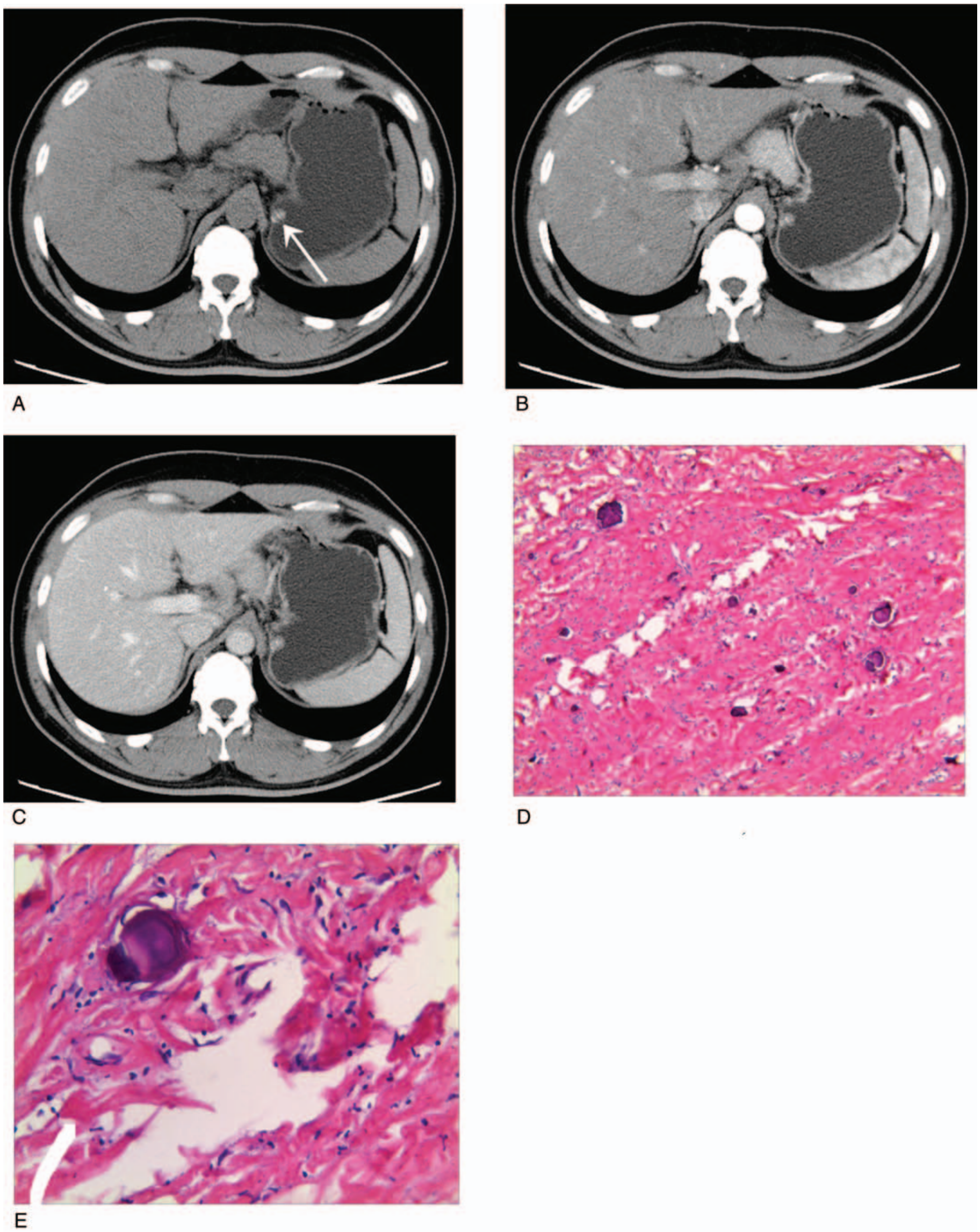

Figure 4. A 30-year-old man with a gastric CFT. Axial (A) unenhanced CT scan depicts a round endophytic mass at lesser curvature of the gastric fundus (↑); furthermore, confluent and coarse calcifications can be seen on the periphery and in the center of the tumor. Axial (B) contrast-enhanced CT scan shows a mildly enhanced mass in the arterial phase. Axial (C) contrast-enhanced CT scan shows a moderately enhanced mass in the portal venous phase. (D) Round, oval and irregular calcifications within the lesion (Hematoxylin & Eosin, × 100). (E) Psammomatous calcifications and lymphoplasmacytic follicles at the periphery or central of the lesion (Hematoxylin & Eosin, × 400).

Our study has several limitations. First, only one type of gastric mesenchymal tumor was evaluated, and no comparative analysis with other gastric mesenchymal tumors was conducted. Second, because of the retrospective nature of this study, data collection had not involved multiple standardized CT protocols, which resulted in image quality bias. Additionally, due to limited number of cases, the clinical values of some CT features require confirmation in further studies with larger samples. Finally, because patients from only 2 centers were analyzed, ethnic and regional uniformity were inevitable, and thus potential ethnic and regional differences could not be reflected.

In conclusion, gastric CFTs commonly occur in the young- or middle-aged female patients and possess a small size, regular shape, unenhanced CT attenuation value similar with the same-transect soft tissue and mild-to-moderate enhancement, however, all these clinical and CT features are not specific, except for the confluent and coarse calcifications.

Table 3

Quantitative CT findings of gastric CFTs.

Case No.	LAD (CM)	SAD (CM)	Ctu (HU)	Ctu-ES (HU)	AP (HU)	PP (HU)	DEAP (HU)	DEPP (HU)
1.	1.6	1.3	57.4	55.3	63.1	76.8	5.7	29.4
2.	1.1	0.9	60.1	57.4	95.0	97.1	34.9	37.0
3.	1.7	1.4	63.3	56.7	79.3	99.7	16.0	36.4
4.	1.6	1.2	59.2	58.1	72.6	67.9	13.4	20.7
5.	1.1	1.0	57.1	62.5	70.2	92.3	13.1	35.2
6.	1.0	0.9	48.7	62.2	91.7	85.6	43.0	36.9
7.	2.9	2.7	71.0	47.8	76.4	79.3	5.4	8.3
M ± SD	1.6 ± 0.7	1.3 ± 0.6	60.2 ± 6.3	56.7 ± 4.7	78.3 ± 11.5	85.5 ± 11.6	18.8 ± 14.5	29.1 ± 10.9

For the quantitative analysis, dates are means ± standard deviations. AP = arterial phase, CFT = calcifying fibrous tumor, CM = centimeter, CT = computed tomography, Ctu = CT attenuation value of unenhanced phase, DEAP = degree of enhancement in the arterial phase, DEPP = degree of enhancement in the portal venous phase, ES = erector spinae, HU = Hounsfield unit, LAD = long axis diameter, PP = portal venous phase, SAD = short axis diameter.

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Software: Jian Wang.
Writing – original draft: Jian Wang, Weiqun Ao.
Writing – review & editing: Jian Wang, Guangzhao Yang.

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