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Endoscopic Ultrasonographic Characteristics of Gastric Schwannoma Distinguished from Gastrointestinal Stromal Tumor

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Background/Aims: Gastric schwannoma (GS), a rare neurogenic mesenchymal tumor, is usually benign, slow-growing, and asymptomatic. However, GS is often misdiagnosed as gastrointestinal stromal tumors (GIST) on endoscopic and radiological examinations. The purpose of this study was to evaluate EUS characteristics of GS distinguished from GIST.
Methods: A total of 119 gastric subepithelial lesions, including 31 GSs and 88 GISTs, who were histologically identified and underwent EUS, were enrolled in this study. We evaluated the EUS characteristics, including location, size, gross morphology, mucosal lesion, layer of origin, border, echogenic pattern, marginal halo, and presence of an internal echoic lesion by retrospective review of the medical records.
Results: GS patients comprised nine males and 22 females, indicating female predominance. In the gross morphology according to Yamada's classification, type I was predominant in GS and type III was predominant in GIST. In location, GSs were predominantly located in the gastric body and GISTs were predominantly located in the cardia or fundus. The frequency of 4th layer origin and isoechogenicity as compared to the echogenicity of proper muscle layer was significantly more common in GS than GIST. Although not statistically significant, marginal halo was more frequent in GS than GIST. The presence of an internal echoic lesion was significantly more common in GIST than GS.
Conclusions: The EUS characteristics, including tumor location, gross morphology, layer of origin, echogenicity in comparison with the normal muscle layer, and presence of an internal echoic lesion may be useful in distinguishing between GS and GIST. **(Korean J Gastroenterol 2015;65:21-26)**

Key Words: Endoscopy; Ultrasonography; Stomach; Schwannoma; Gastrointestinal stromal tumors

INTRODUCTION

Subepithelial lesions of the stomach are found incidentally, occurring in approximately 0.36% of screening upper endoscopy. Most gastric subepithelial lesions are mesenchymal tumors. The entities responsible for mesenchymal tumors of the stomach include gastrointestinal stromal tumor (GIST), leiomyoma, leiomyosarcoma, lipoma, schwannoma, and so on. Of these, GIST is the most common mesenchymal tumor of the stomach with a malignant potential.[1,2]

Gastric schwannoma (GS) is a rare neurogenic mesenchymal tumor. This tumor is usually benign, slow-growing,

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and asymptomatic, with extremely low malignant potential and an excellent prognosis after surgical resection.[3,4] However, GS is often misdiagnosed as GIST on endoscopic and radiological examinations. Therefore, accurate differential diagnosis of GS and GIST has important prognostic and therapeutic implications.

EUS is the most reliable procedure for assessing the tumor's layer of origin, the exact size of the lesion, morphologic features, differential diagnosis, classification, and follow up of gastric subepithelial lesions. Therefore, a better understanding of its unique features for differential diagnosis may be helpful in providing effective intervention strategies and guide selection of appropriate therapy.

To date, case series describing EUS features in only four GS patients, respectively, have been reported.[5,6] The purpose of this study was to evaluate EUS characteristics of GS distinguished from GIST.

SUBJECTS AND METHODS

We searched the pathologic database at Department of Gastroenterology, Chonnam National University Hwasun Hospital (Hwasun, Korea) to find patients with histologically proven gastric subepithelial lesions between January 2004 and December 2013. A total of 573 gastric subepithelial lesions, including 283 GISTs (49.4%), 90 leiomyomas (15.7%), 60 ectopic pancreas (10.5%), 31 schwannomas (5.4%), and 15 carcinoids (2.6%) were identified histologically by surgical resection. Among them, patients with GS and GIST who underwent EUS examination were enrolled in this study; EUS-guided fine-needle aspiration or trucut biopsy was not performed. The final study population consisted of 31 GS and 88 GIST patients. Subsequently, we searched the medical database and the following information was retrieved for analysis: (1) age, sex, and symptoms of the patients, (2) EUS characteristics including location, size, gross morphology classified according to Yamada's classification,[7] mucosal lesion, layer of origin, border, echogenic pattern including echogenicity, homogenecity and comparison to the echogenicity of proper muscle layer, marginal halo, and presence of an internal echoic lesion including cyst, hyperechogenic spot, and calcification. This study was reviewed and approved by the Institutional Review Board of Chonnam National University Hwasun Hospital, and written informed consent was obtained from all participating subjects for retrospective review of the patients' medical records and images. EUS examination was performed using a mechanical radial-scanning-echoendoscope (GF-UM2000; Olympus, Tokyo, Japan). The scanning frequency ranged from 5 to 20 MHz. All examinations were performed by 1 of 4 experienced endosonographers who had performed more than 150 diagnostic EUS examinations.

The SPSS software version 15.0 (SPSS Inc., Chicago, IL, USA) was used for data analysis employing the χ^2 and Fisher's exact test. A value of $p < 0.05$ was considered statistically significant.

RESULTS

1. Baseline characteristics of GS and GIST patients

The final enrolled population consisted of 31 GS and 88 GIST patients. The baseline characteristics of enrolled subjects, including age, sex, and gastrointestinal (GI) symptoms are described in Table 1. The mean age of GS patients was 58.1±9.2 (mean±SD) with a range from 40 to 73 years. GS patients comprised nine males (29.0%) and 22 females (71.0%), indicating female predominance. Most GS patients were asymptomatic (83.9%) and five patients (16.1%) presented with epigastric discomfort. However, no significant differences in the baseline characteristics were observed between the GS and GIST groups.

2. Endoscopic characteristics of GS and GIST

The endoscopic characteristics of GS and GIST patients are summarized in Table 2. All GSs were round to ovoid shape and there was no lobulated shape. The five GSs (16.1%) had

Table 1. Baseline Characteristics of the Patients with GSs and GISTs of the Stomach

Variable	GS (n=31)	GIST (n=88)	p-value
Gender			0.092
Male	9 (29.0)	42 (47.7)	
Female	22 (71.0)	46 (52.3)	
Age (yr)	58.13±9.219	58.09±11.433	0.987
Gastric symptom			0.455
Absent	26 (83.9)	67 (76.1)	
Present	5 (16.1)	21 (23.9)	

Values are presented as n (%) or mean±SD.
GS, gastric schwannoma; GIST, gastrointestinal stromal tumor.

mucosal lesions such as central ulceration (n=2), central depression (n=1), erosion (n=1), and umbilication (n=1). In the gross morphology of GSs according to Yamada's classification, 16 (51.6%) were type I, 12 (38.7%) type II, and 3 (9.7%) type III; 28 (90.3%) GSs were located in the gastric body (19 [61.3%] in the greater curvature [GC] and 9 [29.0%] in the lesser curvature of the body), followed by antrum (n=2) and cardia or fundus (n=1). In GISTs patients, the gross morphology according to Yamada's classification was predominant type III (n=35, 39.8%) and the most common location was the cardia or fundus. Comparing GSs with GIST patients, the gross morphology and location was significantly different (p=0.030 and p < 0001, respectively) (Fig. 1).

Table 2. Endoscopic Features of the Patients with GSs and GISTs of the Stomach

Variable	GS (n=31)	GIST (n=88)	p-value
Shape			0.062
Round to ovoid	31 (100)	78 (88.6)	
Lobulated	0 (0)	10 (11.4)	
Mucosal lesion			1.000
Present	5 (16.1)	14 (15.9)	
Absent	26 (83.9)	74 (84.1)	
Morphology (Yamada's classification)[a]			0.030
Type I	16 (51.6)	26 (29.5)	
Type II	12 (38.7)	35 (39.8)	
Type III	3 (9.7)	27 (30.7)	
Type IV	0 (0)	0 (0)	
Location			0.001
Body, GC	19 (61.3)	21 (23.9)	
Body, LC	9 (29.0)	24 (27.3)	
Cardia/fundus	1 (3.2)	37 (42.0)	
Antrum	2 (6.5)	6 (6.8)	

Values are presented as n (%).
[a]Yamada type I is elevated, with an indistinct border; Type II is elevated with a distinct border at the base but no notch; Type III is elevated, but no peduncle; Type IV is pedunculated and elevated.
GS, gastric schwannoma; GIST, gastrointestinal stromal tumor; GC, greater curvature; LC, lesser curvature.

3. Endosonographic characteristics of GS and GIST

The endosonographic characteristics of GS and GIST patients are summarized in Table 3. The mean size of GSs was 26.0±8.4 (mean±SD) with a range from 12 to 42 mm. All GSs originated from the fourth layer, with a connection between the tumor and the muscularis propria and had a distinct border. In echogenic patterns of the GSs, 17 (54.8%) exhibited homogeneous hypoechogenicity and 14 (45.2%) were heterogeneous hypoechogenicity; 22 GSs (71.0%) had a marginal hypoechoic halo; 22 GSs (71.0%) exhibited isoechogenicity and 9 (29.0%) exhibited hyperechogenicity, compared to the echogenicity of surrounding proper muscle layer (Fig. 1B). Only three GSs had internal echoic lesions including cystic change (n=2) and hyperechogenic spot (n=1). GISTs originated from the 4th layer in 76 patients (86.4%) and 3rd layer in 12 patients (13.6%); 42 GISTs (47.7%) exhibited isoechogenicity and 46 (52.3%) exhibited hyperechogenicity, compared to the echogenicity of the normal proper muscle layer (Fig. 2B). The frequency of 4th layer origin and isoechogenicity compared to the echogenicity of the normal proper muscle layer was significantly more common in GS than GIST (p=0.035 and p=0.036, respectively); 44 GISTs (50.0%) had a marginal hypoechoic halo. Although not statistically significant, the frequency of marginal halo was greater in GS than GIST (p=0.058). The presence of an internal echoic lesion including cystic change (n=14, 15.9%), hyperechogenic spot (n=22, 25.0%), and calcification (n=9, 10.2%) was significantly more common in GIST than GS (p=0.036).

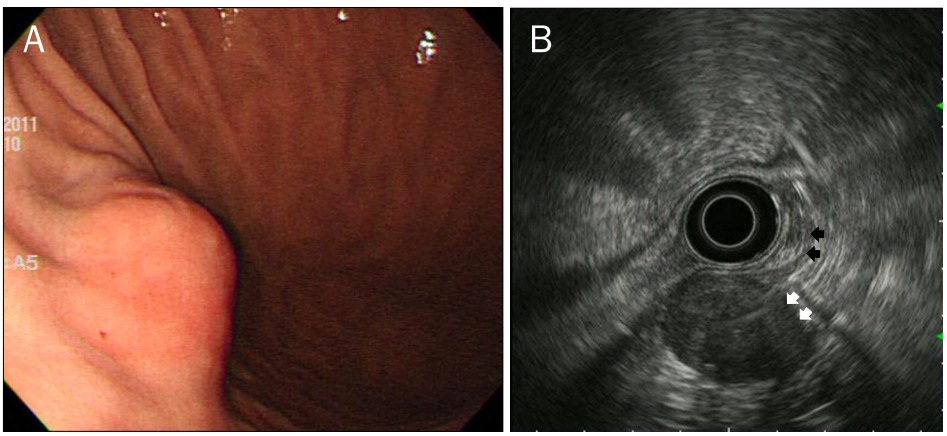

Fig. 1. Endoscopic (A) and endosonographic (B) findings in a 59-year-old woman with a gastric schwannoma. (A) Endoscopy shows a submucosal elevated lesion with type I morphology according to Yamada's classification in the greater curvature of the body. (B) On EUS, the mass is homogeneous and its echogenicity is similar to that of the normal proper muscle layer (black arrows). It measures 32.0×21.0 mm in size and a marginal halo (white arrows) is observed.

Table 3. Endoscopic Ultrasonography Features of the Patients with GSs and GISTs of the Stomach

Variable	GS (n=31)	GIST (n=88)	p-value
Size (mm)	26.03±8.373	25.20±15.665	0.780
Layer			0.035
3rd	0 (0)	12 (13.6)	
4th	31 (100)	76 (86.4)	
Border			0.110
Regular	31 (100)	80 (90.9)	
Irregular	0 (0)	8 (9.1)	
Marginal halo			0.058
Absent	9 (29.0)	44 (50.0)	
Present	22 (71.0)	44 (50.0)	
Echogenicity			0.408
Homogeneous hypoechoic	17 (54.8)	40 (45.5)	
Heterogeneous hypoechoic	14 (45.2)	48 (54.5)	
Echogenicity in comparison with the surrounding muscle echo			0.036
Isoechoic	22 (71.0)	42 (47.7)	
Hyperechoic	9 (29.0)	46 (52.3)	
Internal echoic lesion			
Cystic change	1 (3.2)	14 (15.9)	0.112
Hyperechogenic spots	2 (6.5)	22 (25.0)	0.036
Calcification	0 (0)	9 (10.2)	0.110

Values are presented as mean±SD or n (%).
GS, gastric schwannoma; GIST, gastrointestinal stromal tumor.

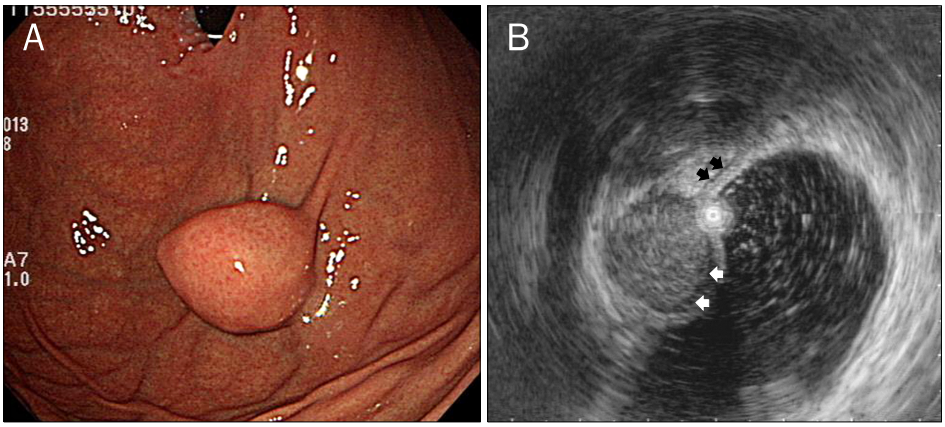

Fig. 2. Endoscopic (A) and endosonographic (B) findings in a 66-year-old woman with a gastrointestinal stromal tumor. (A) Endoscopy shows a submucosal elevated lesion with type III morphology according to Yamada's classification in the cardia. (B) On EUS, the mass is homogeneous and its echogenicity is higher than that of the normal proper muscle layer (black arrows). It measures 20.0×16.0 mm in size and a marginal halo (white arrows) is observed.

DISCUSSION

Schwannomas are spindle cell mesenchymal tumors originating from any nerve having a Schwann cell sheath. In the GI tract, GISTs comprise the largest group of mesenchymal tumors, whereas schwannomas are rare, with reported prevalence ranging from 3.3-12.8% of all GI mesenchymal tumors.[4,8,9] In our study, prevalence of GS was 5.4% (31 GS patients among a total of 573 patients) and the tumors occurred predominantly in older adults with a marked female predominance. The majority of GSs follow a benign clinical course and malignant transformation is extremely rare, as a few cases have been reported in the literature.[10,11]

In clinical practice, preoperative differential diagnosis between mesenchymal tumors of the stomach is usually difficult. GSs are rare benign mesenchymal tumors of the stomach. However, because of different prognostic and therapeutic implications, it is necessary to differentiate GSs from other mesenchymal tumors of the stomach, particularly GISTs with malignant potential. Endoscopically, GSs appear as elevated lesions, with or without central ulcers. In several studies, the location of the tumors was predominant in GC of

the body of the stomach.[4,6] In our study, GSs showed statistically significant predominance in the GC of the body, compared with GISTs. In addition, previous studies showed that GSs had an exophytic growth pattern rather than an endoluminal growth pattern.[12-14] In our study, the gross finding according to Yamada's classification was a predominance of type I, classified by an elevated lesion with an indistinct border and it was statistically significant, compared with GISTs. There are no previous reports describing the gross finding according to Yamada's classification in GSs or GISTs. Although our study population was relatively small, which might influence some results, this finding may be the endoscopic feature, reflecting GSs with an exophytic growth pattern.

The features of GSs on EUS have been described as round submucosal lesions with marginal halo, and homogeneous internal echogenicity without internal echogenic foci, arising from the 4th layer.[6,15] Some reports have suggested that the echogenicity of GSs compared with the normal proper muscle layers may be helpful for differentiating them from GISTs.[5,6] One study suggested that the echogenicity of GSs was much lower than that of the normal proper muscle layers.[6] In other case reports, the internal echogenicity of GSs was heterogeneous and low, but slightly higher than that of muscularis propria, with internal patch high echo.[5] According to our results, isoechogenicity in comparison with the normal proper muscle layer was predominantly found in 71.0% of GSs, whereas hyperechogenicity was predominantly found in 52.3% of GISTs. Pathologically, GISTs have high cellularity with a basophilic appearance on H&E, whereas GSs have moderate overall cellularity.[4,16-18] In addition, the degenerative changes, including hemorrhage, necrosis, and cystic change, which are often seen in soft-tissue schwannomas, were not the common features of GI schwannomas, although these tumors grossly resemble soft-tissue schwannomas.[9] However, hemorrhage, necrosis, and cystic change are the common features in GISTs and calcification is seen in 6% of GISTs.[19] In our study, the presence of an internal echoic lesion including cystic change, hyperechogenic spot, and calcification was significantly more common in GIST than GS. These differences in echogenicity and the presence of an internal echoic lesion between GSs and GISTs might reflect the pathologic differences of cellularity and the structural components of the tumors.

In previous studies a marginal halo, corresponding to histopathologically lymphoid cuff was observed on EUS in GSs and GISTs.[4,15] Recently, although small case series, a marginal halo was found in the majority of GSs.[5,6,15] In our study, marginal halo was found in 71.0% of GSs and 50.0% in GISTs. Although not statistically significant, the frequency of marginal halo was greater in GSs than GISTs.

Our study had several limitations. First, this was a retrospective study comparing the EUS features of GISTs and GSs. In addition, there might have been a potential bias when retrospectively reviewing the EUS photos. Second, although EUS examinations were performed, patients were selected for surgery according to the clinical opinions of the many doctors including internist and surgeon. Third, in addition to the GS, preoperative differentiation between GISTs and gastric leiomyomas is also important. However, the gastric leiomyoma was not included in our study. In previous studies, a marginal halo appeared more frequently in GISTs than in leiomyoma and the echogenicity of the leiomyoma was similar to that of the normal proper muscle layer.[15,20] These results demonstrate that the EUS features of leiomyomas and GSs have many similarities. Therefore, in the future, conduct of large-scale studies should be considered in order to determine the differential diagnostic points of many gastric mesenchymal tumors.

In summary, GSs were predominantly type I according to Yamada's classification and were predominantly located in the gastric body, compared with GISTs. The EUS features such as homogeneous hypoechogenicity, a well-demarcated margin, fourth-layer origination, and lack of cystic change, hyperechogenic spot and calcification, isoechogenicity compared to the echogenicity of normal proper muscle layer may be helpful in differentiation of GSs from GISTs. In our study, a marginal halo was the common feature of GSs, but not an essential one for differentiation GSs from GISTs.

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