A Case of Gastric Granular Cell Tumor: Review of Literature and Features of Endoscopic Ultrasonography

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Granular cell tumor was originally described as granular cell myoblastoma by Abrikossoff. The incidence of GCT in the gastrointestinal tract is low, and most granular cell tumors occur in the esophagus and large bowel. Gastric granular cell tumors are rare and difficult to distinguish from carcinoid tumors by gross endoscopic findings and endoscopic ultrasonography findings. We report a case of gastric granular cell tumor, treated by endoscopic submucosal dissection, and review the endoscopic ultrasonography findings of recently reported gastric granular cell tumors. (**Korean J Helicobacter Up Gastrointest Res 2015;15:59-63**)

Key Words: Granular cell tumor; Endosonography; Stomach

INTRODUCTION

Granular cell tumor (GCT) was described as granular cell myoblastoma by Abrikossoff for the first time in 1926. GCTs are uncommon, usually benign neoplasm that can be located at any sites. The incidence of GCT in the gastrointestinal (GI) tract is low. Most of GI GCTs are in the esophagus and large bowel, but rarely in the stomach.^{1,2} At least 50% of gastric GCTs are associated with synchronous esophageal GCTs and they usually occur in the proximal stomach.³ GCTs arising in the stomach are almost benign, and only a case of malignant gastric GCT was reported.⁴ Histologically, GCTs consist of large polygonal and fusiform cells disposed in compact nests. GCTs are almost positive for S-100 protein and neuron specific enolase (NSE), suggesting that GCTs are derived from Schwann cells.⁵ On the endoscopy, most GCTs appear as sessile, small, yellowish-white in color, and covered by normal appearing mucosa.⁶ Conventional endoscopic findings and EUS findings of carcinoid tumors are similar to

GCTs, therefore differential diagnosis between GCTs and carcinoid tumors is very difficult.⁷ Patti et al.⁸ reported a case of gastric GCT in 2006, and reviewed 5 cases of gastric GCTs. Since 2006, eleven cases of gastric GCT have been reported.⁹⁻¹⁵ Ten cases could be found in the PubMed (US National Library of Medicine) and were written in English^{9,10,12-15} and a single case was written in Korean.¹¹ Among of eleven cases, EUS was performed in six cases.^{11,12,15} We report a case of a 31-year-old man with GCT of stomach, seemed like carcinoid, and we review the endoscopic findings and EUS findings of recent gastric GCT cases.

CASE REPORT

A 31-year-old man was admitted to our hospital for further evaluation of a gastric subepithelial lesion. He underwent upper GI endoscopy for a health check-up at local medical center. Endoscopic examination of local medical center revealed a 6 mm sized subepithelial lesion in the cardia of stomach. An endoscopic biopsy was performed, and histopathological examination of endoscopic biopsy showed a partially some large polygonal cells with eosinophilic granular cytoplasm in lamina propria. It suggested a GCT, and then he was referred to Pusan

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National University Yangsan Hospital. He had no significant medical history. At the time of admission, AST was 50 IU/L, and ALT was 99 IU/L. Other laboratory studies, including complete blood count, coagulation studies, electrolytes, and creatinine, were within normal limit. His height and weight was 171.9 cm and 91.4 kg, and his body mass index was 30.93 kg/m². He had no cause of liver enzyme elevation except obesity. A CT of

abdomen showed slightly high density of liver, it was considered fatty liver.

Upper GI endoscopy revealed a less than 10 mm sized, yellow-whitish, hard subepithelial lesion in the cardia of the stomach (Fig. 1). There was no specific lesion in the esophagus. EUS was subsequently performed for tumor invasion depth (Fig. 2). EUS showed a 6×4 mm sized, smooth, well demarcated, homogeneous hypoechoic solid lesion in 2nd and 3rd layer. Because there was no evidence of muscle proper layer invasion, ESD was performed for treatment (Fig. 3). Histopathologically, the tumor mainly located in the submucosa, and extended to mucosa. It formed solid nests of cells with abundant eosinophilic granular cytoplasm. Immunohistochemical stain of resected specimen showed that the cells were positive for S-100 protein (Fig. 4). These findings are typical of GCT. The patient made an uneventful post-ESD recovery and he was discharged on 2nd day after ESD.

DISCUSSION

GCTs were defined by Abrikossoff for the first time in 1926. GCT was described as a granular cell myoblastoma, since it was reported as a tumor arising from muscle in the tongue.¹⁶ Recently, GCTs were thought to be derived from neural origin.⁵

Fig. 1. Endoscopy revealed a yellow-whitish, hard and mobile subepithelial lesion in the cardia of the stomach. The tumor was difficult to distinguish from carcinoid tumor.

Fig. 2. EUS revealed a smooth, well demarcated, homogeneous hypoechoic solid lesion in 2nd and 3rd layer.

Fig. 3. The resected specimen showed yellow-whitish inner surface.

Fig. 4. (A) A large, polygonal tumor cells mainly located in the submucosa, and extended to mucosa. (H&E, $\times 12$). (B) The tumor cells were well-demarcated, and had abundant eosinophilic granular cytoplasm with small round nuclei (H&E, $\times 200$). (C) The tumor cells were positive for S-100 protein (S-100 stain, $\times 200$).

GCTs are uncommon, usually benign neoplasm that can be located at any sites, although they are usually in the skin or soft tissues. They are usually found in the oral cavity (40%), skin and subcutaneous tissue (30%), breast (15%), or respiratory tract (15%).² The reported incidence of multifocal GCT ranges between 5 and 16%.¹⁶ The incidence of GCT in the GI tract is approximately 8%, and most of GI GCTs are in the esophagus and large bowel.¹ The GCTs of stomach are rare among GI GCTs. Only 24 patients with gastric GCT had been reported until 1995, and five more cases had been reported until 2006.^{6,8} Since 2006, eleven more cases have been reported (Table 1).⁹⁻¹⁵

GCTs of GI tract are usually benign, although a case of malignant gastric GCT was reported in 1996.⁴ Most malignant GCTs are larger than 4 cm, and six histologic criteria were assessed: necrosis, spindling, vesicular nuclei with large nucleoli, increased mitotic activity (>2 mi-

tos/10 high power fields), high nuclear to cytoplasmic ratio, and pleomorphism.¹⁷

GCTs consist of large polygonal and fusiform cells disposed in compact nests, and GCTs have abundant eosinophilic granular cytoplasm with small round nuclei.⁶ GCTs are almost positive for S-100 protein and NSE, therefore GCTs are believed to be derived from Schwann cells.^{5,18}

On the endoscopy, gastric GCTs can be mistaken for gastric carcinoid tumors. However, most gastric carcinoid tumors are usually multiple lesions and often appear small polypoid lesion with central depression or central ulcer.¹⁹ On the other hand, most gastric GCTs are a solitary lesion, and appear a yellowish-white lesion without central depression or central ulcer in our review.⁹⁻¹⁵ These endoscopic features can be helpful to distinguish gastric GCTs from gastric carcinoid tumors.

On the EUS, gastric GCTs usually appear as hypo-

Table 1. Characteristics of Reported Eleven Gastric Granular Cell Tumor since 2006

Case	Sex	Age (yr)	Size (mm)	Treatment	EUS findings	Esophageal granular cell tumor
Rekha and Srinivas ⁹	Male	30	20	Endoscopic resection	No mention	No
John et al. ¹⁰	Female	30	No mention	Operation	No mention	Yes
Park et al. ¹¹	Female	29	13×10	Endoscopic resection	2nd, 3rd layer, homogenous, hypoechoic, ill defined	No
Monahan et al. ¹²	Male	49	8	Endoscopic resection	3rd layer, homogenous, hypoechoic, well defined	No
Pertile et al. ¹³	Male	45	20×13	Operation	No mention	No
Min et al. ¹⁴	Male	49	10	Endoscopic resection	No mention	No
Kahng et al. ¹⁵	Female	33	17	Endoscopic resection	2nd, 3rd layer, Homogenous, hypoechoic, well defined	No
Kahng et al. ¹⁵	Female	76	10	Endoscopic resection	No mention	No
Kahng et al. ¹⁵	Female	52	12	Endoscopic resection	2nd, 3rd layer, Heterogenous, hypoechoic, well defined	No
Kahng et al. ¹⁵	Female	46	13	Endoscopic resection	3rd layer, homogenous, hypoechoic, ill defined	No
Kahng et al. ¹⁵	Male	57	7	Endoscopic resection	2nd, 3rd layer, homogenous, hypoechoic, well defined	No

Table 2. Comparison of Endoscopic and EUS Findings between Gastric Granular Cell Tumors and Carcinoid Tumors

	Granular cell tumor	Carcinoid tumor
Endoscopic findings		
Number	Solitary	Multiple
Surface	Yellowish-white in color, normal-appearing mucosa	Erythematous depression or central ulceration
EUS findings		
Homogeneity	Relatively inhomogenous than carcinoid	Homogenous
Echogenicity	Hypoechoic, but more echogenic than carcinoid	Hypoechoic

echoic, homogenous lesions with smooth margins arising from the mucosa and/or submucosa.⁶ These EUS findings of gastric GCTs are similar to those of gastric carcinoid tumors, therefore differential diagnosis between GCTs and carcinoid tumors is very difficult.⁷ For this reason, we reviewed EUS findings of recent gastric GCTs since 2006. EUS were performed in the 6 cases among the recent 11 cases.^{11,12,15} When we observed closely the previous cases, EUS findings of recent gastric GCTs were slightly different from those of gastric carcinoid tumors. The EUS findings of gastric GCTs were relatively inhomogenous and more echogenic, compared with gastric carcinoid tumors. These EUS findings can be helpful to distinguish the gastric GCTs from the gastric carcinoid tumors as well as the endoscopic features (Table 2). Furthermore, EUS can be used to determine the invasion depth of gastric GCTs. If EUS can determine that gastric GCTs are limited to the

submucosal layers, endoscopic resection has proven to be a safe and effective treatment for GCTs in the GI tract.¹⁵

Gastric GCTs are known to be strongly associated with synchronous esophageal GCT, although just one case was associated with synchronous esophageal GCT among recent 11 cases^{3,8} and our case was not associated with synchronous esophageal GCT. Therefore, if gastric GCT is diagnosed, a careful endoscopic inspection will be required for evaluation of synchronous esophageal GCTs.

Most of gastric subepithelial lesions such as leiomyoma are difficult diagnosed by endoscopic forcep biopsy. However, GCTs usually locate in the deep mucosa or submucosa, which makes GCT possible to be diagnosed by endoscopic forcep biopsy, up to 83% of patients.²⁰ In our case, endoscopic forcep biopsy could diagnose the lesion as GCT.

We report a case of a 31 year old man with GCT of

gastric cardia, successfully diagnosed by endoscopic forcep biopsy and treated by endoscopic submucosal dissection, and we review the endoscopic and EUS findings of recent gastric GCT cases.

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