Gastric granular cell tumor in a youth excised by endoscopic submucosal dissection : A case report and literature review

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Abstract

Granular cell tumors (GCTs) usually develop in patients aged 30–50 years in the skin, tongue, and mammary gland, with 5–9% of GCTs occurring on the esophagus, ascending colon, and cecum. We report a case of gastric GCT in a 16-year-old male who presented with nausea and abdominal discomfort. Esophagogastroduodenoscopy (EGD) revealed an elastic hard and yellowish submucosal tumor of the gastric cardia anterior wall. GCT was suspected upon biopsy ; after total endoscopic submucosal dissection, histology of the resected tumor confirmed the diagnosis. Endoscopic treatment should be considered in youths with GCT. (Acta gastroenterol. belg., **2017**, 80, **317-319**).

Key word : Gastric granular cell tumor (GCT), stomach, endoscopic ultrasonography (EUS), endoscopic submucosal dissection (ESD).

Introduction

Granular cell tumors (GCTs) usually develop in the skin, tongue, and mammary gland. About 5%-9% of GCTs occurring in the gastrointestinal tract. GCTs of the gastrointestinal tract commonly develop in the esophagus and the right side of the colon, particularly the ascending colon and cecum (1). Generally, GCTs affect patients aged 30-50 years, and rarely occur in the stomach (2). Histologically, GCTs consist of sheets of polygonal cells that stain positive for S-100 protein and are arranged in bundles, with rich eosinophilic granules in the cytoplasm. Malignant GCT is diagnosed by pathological examination, local recurrence, or a rapidly growing tumor. However in several cases malignancy is difficult to diagnose based on an endoscopic biopsy specimen (2). There is currently no established therapy for treating GCTs. Only two cases were reported where the tumor had malignant potential. GCTs had been excised by operation previously. But recently endoscopic treatment including endoscopic mucosal resection, or endoscopic submucosal dissection (ESD) was used (2). Herein we present the youngest case of gastric GCT that was diagnosed by endoscopic biopsy and completely resected by EGD.

Case Report

A 16-year-old male was referred to our hospital because of nausea and abdominal discomfort. He had no medical or family history of gastrointestinal issues and did not smoke cigarettes or drink alcohol. His general physical condition was good and both physical and laboratory examinations were almost normal (Table 1). Esophagogastroduodenoscopy (EGD) revealed a submucosal tumor presenting as an elastic hard and yellowish lesion at the anterior wall of the cardia of the stomach (Fig. 1A). The tumor was estimated to be approximately 10 mm in diameter that was covered with normal mucosa and had a central depression. Endoscopic ultrasonography (EUS) revealed that the tumor was localized in the second and third mucosal layers, had not infiltrated into the fourth layer, and showed an internal echo pattern that was heterogeneously hypoechoic (Fig. 1B). An endoscopic tumor biopsy revealed sheets of polygonal cells arranged in bundles with rich eosinophilic granules in the cytoplasm and positive S-100 protein staining. The tumor was suspected to be a gastric GCT. In general, GCT has a low risk of malignancy. However, the patient was young and GCT may become malignant in the future, therefore we decided to remove the tumor by ESD for excisional biopsy. During ESD, the tumor did not adhere to the muscle layer and was easily peeled away and completely dissected. The dissected tumor size was 15 × 11 mm. The lesion was mainly located in the submucosa and the portion in the lamina propria showed negative tumor margins. As revealed by the biopsy, the tumor consisted with sheets of polygonal cells arranged in bundles with rich eosinophilic granules in the cytoplasm on hematoxylin and eosin staining (Fig. 2A). The cytoplasmic granules were positive for both S-100 protein (Fig. 2B) and periodic acid-Schiff (PAS) staining. In addition, immunohistochemical staining for c-kit, CD34 and synaptophysin were all negative. Furthermore, 1.9% of the tumor cells were positive for Ki-67 staining, and there was no evidence of dyskaryosis or necrosis. The tumor was dissected complete en bloc. The tumor was diagnosed as a non-malignant GCT. After

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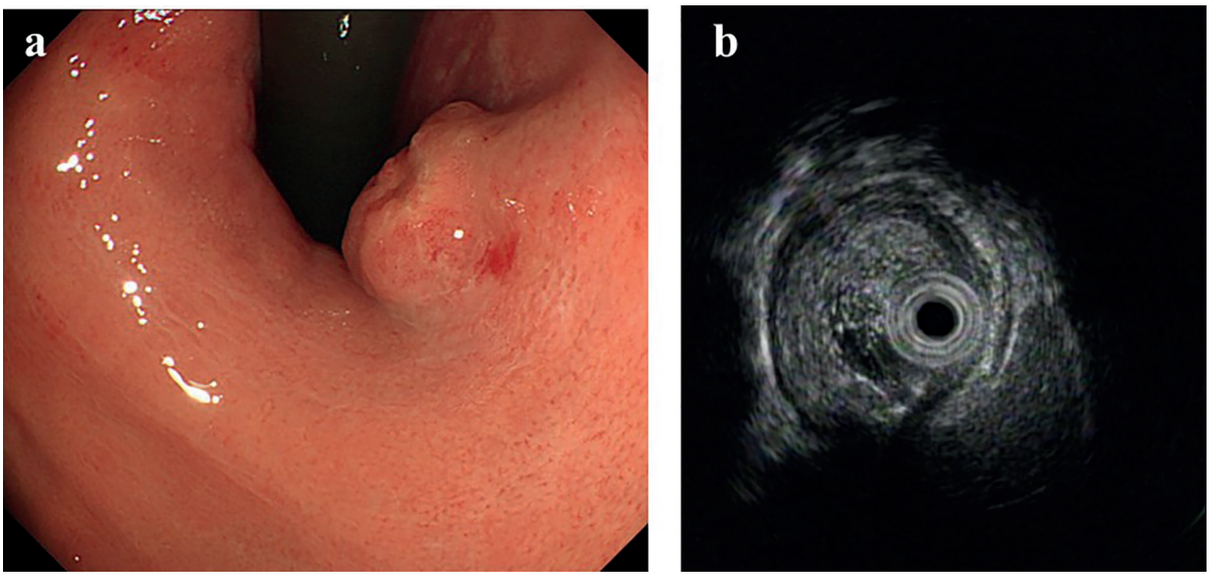

Fig. 1. — (a) Esophagogastroduodenoscopy revealed a yellowish, elastic, hard submucosal tumor at the anterior wall of the cardia (proximal stomach) approximately 10 mm in diameter with a central depression. (b) Endoscopic ultrasonography located the tumor at the second and third layer. The tumor line was clearly demarcated and the internal echo pattern was heterogeneously hypoechoic.

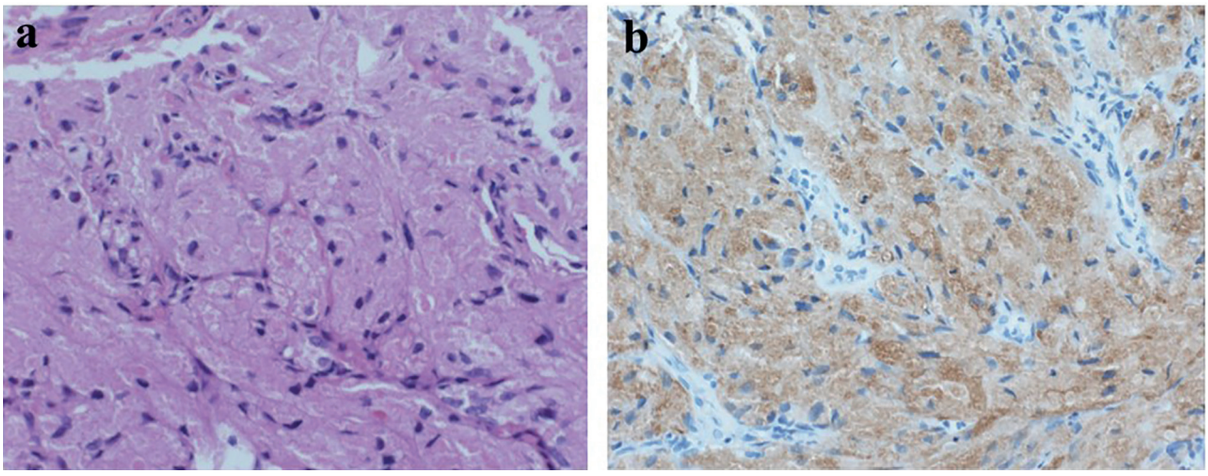

Fig. 2. — (a) Hematoxylin and eosin staining of slide-mounted tumor tissue revealed sheets of polygonal cells arranged in bundles with rich eosinophilic granules in the cytoplasm. (magnification × 40). (b) Tumor S-100 protein staining was positive. (magnification × 40).

ESD was performed, the patient remained stable with no recurrence for one year.

Discussion

GCT, first reported by Abrikossff in 1926 (3), usually occurs in the skin, tongue, mammary gland, or digestive organs, with only 5-9% of GCT developing in the gastrointestinal tract (4,5). And the tumor developed in the stomach is less than 1% (6,7). GCT is thought to originate from Schwann cells (8). Histologically, GCTs are comprised of sheets of polygonal cells arranged in bundles enriched with PAS-positive, eosinophilic granules in the cytoplasm, and S-100 protein and NSE were positive on immunohistochemical staining (9. 10). In the present case, all classic GCT features were observed in the resected specimen, resulting in a final diagnosis of a gastric GCT. GCTs are commonly difficult to distinguish from other submucosal tumors, including carcinoid tumors, gastrointestinal stromal tumors (GISTs), heterotopic pancreas, and lipomas. Carcinoid tumors show an elastic hard and yellowish lesion by EGD, and the tumor is typically localized in the third mucosal layer with a heterogeneously hypo-internal

echo pattern by EUS. GIST is usually localized in the fourth mucosal layer, and EUS internal echo pattern is heterogeneously hypoechoic. Heterotopic pancreas presents as a tumor localized in the third mucosal layer, with a hypoechoic internal echo pattern and finely scattered hyperechoic spots. Finally, lipoma is localized to the third layer, and the EUS internal echo pattern is homogeneously hyperechoic. In the present case, the tumor was suspected as gastric GCT by endoscopic biopsy, which is useful to perform for confirmation of the diagnosis. However, many cases are difficult to diagnose by endoscopic biopsy. In our summarized cases, 43% couldn't diagnose. Recently, EUS-guided fine needle aspiration (FNA) was used for diagnosing submucosal tumors (SMTs), and it is reported that EUS-FNA had high SMT diagnostic capability (11). Therefore, EUS-FNA may also be useful for diagnosing GCT. Only two cases of malignant GCT have been reported previously (12, 13). Fanburg et al. reported 6 histological criteria for differentiating atypical or malignant GCT (14) : (1) an increase in the nuclear to cytoplasmic ratio, (2) nuclear pleomorphism, (3) necrosis, (4) spindling of tumor cells, (5) vesicular nuclei with prominent nucleoli, and (6) a mitotic count of more than 2 per 10 high power microscopy fields. Gastric GCTs are divided into 3 classifications : benign, 0 ; atypical, 1-2 ; and malignant, 3-6. In this case, we diagnosed this tumor as a benign GCT because not all diagnostic criteria fit with another diagnosis. In addition, it was reported that malignant GCTs are highly proliferative, which is indicated by >10% of Ki-67 and >50% of p53 positive immunohistochemical staining. Pathological examination is thought to be indispensable for diagnosis of malignancy. Since 1969, reports of approximately 60 gastric GCT cases have appeared in the PubMed literature database. We summarized 48 cases for which details were accessible (2,12). These gastric GCT features are presented in Table 2. The average patient age was 49.0 years, with our case being the youngest to be reported. And 68.2% were men. About 37.2% of GCT patients complained of abdominal discomfort. In several cases, there were no distinct symptoms and the tumor was detected accidentally. In the present case, it is thought that the patient had abdominal discomfort which is related to GCT. The tumors tended to be approximately 10-20 mm in diameter and located at the middle body of the stomach. Tumors mainly occupied the submucosal layers, and EUS finding were hypoechoic. Approximately 27% of gastric GCTs have been diagnosed by endoscopic biopsy and approximately 4.5% of them were malignant (12,13). There is currently no established therapeutic approach to treating gastric GCT. Because only a few reported cases were malignant, it is thought that excision is the primary required therapy. Previously, these tumors were mainly excised by operation ; however, recently, the method of choice for tumor excision has been either endoscopic mucosal resection (EMR) or ESD. However, it was reported that if the tumor has invaded the muscle layer, alternative or additional courses of treatment should be carefully considered. EUS may be a useful aid in this decision. Treatment varies depended on the value of tumor. The size of tumor excised by EMR and ESD were less than 20mm. 66.7% of the tumor excised by EMR and ESD. On the other hand, more than 20 mm the size of tumors operated in all cases. It is thought that great tumors operated to become malignant (5).

Conclusion

This is the youngest case of gastric GCT to be excised by ESD. GCT seldom has malignant potential. For the current case, because the patient was young and GCT may become malignant, we decided to excise the tumor for excisional biopsy.

References

1. NAKANOME T., YOKOYAMA K., TAKEUCHI H. *et al*. Rectal granular-cell tumor difficult to distinguish from carcinoid tumor. *Dig. Endosc*., 2010, **22** : 325-328.
2. WAKASUGI A.,TAKAHASHI H., OSTUKA T. *et al*. Endoscopically Resected Granular Cell Tumor of the Stomach. *Dig. Endosc*., 1996, **8** : 328-331.
3. ABRIKOSSOFF A., UBER MYOMA. ausgehend von der quergestreiften wilkurlichen Muskulatur. *Virchow. Arch. Pathol. Anat*., 1926, **260** : 215-233.
4. MAEKAWA H., MAEKAWA T., YABUKI K. *et al*. Multiple esophagogastric granular cell tumors. *J. Gastroenterol*., 2003, **38** : 776-780.
5. DAVID O., JAKATE S., Multifocal granular cell tumor of the esophagus and proximal stomach with infiltrative pattern a case report and review of the literature. *Arch. Pathol. Lab. Med*., 1999, **123** : 967-973.
6. JOHNSTON J., HELWIG E.B. Granular cell tumors of the gastrointestinal tract and perianal region : a study of 74 cases. *Dig. Dis. Sci*., 1981, **26** : 807-816.
7. AN S., JANG J., MIN K. *et al*. Granular cell tumor of the gastrointestinal tract : histologic and immunohistochemical analysis of 98 cases. *Hum. Pathol*., 2015, **46** : 813-819.
8. MUKAI M. Immunohistochemical localization of S-100 protein and peripheral nerve myelin proteins (p2 protein, p0 protein) in granular cell tumor. *Am. J. pathol*., 1983, **112** : 139-146.
9. NIE L., XU G., WU H. *et al*. Granular cell tumor of the esopagus : a clinicopathilogical study of 31 cases. *Int. Clin. Exp. Pathol*., 2014, **7** : 4000-4007.
10. ZHANG M., SUN Z.Q., ZOU X.P. Esophageal granular cell tumor : Clinical, endoscopic and histological features of 19 cases. *Oncol. Lett*., 2014, **8** : 551-555.
11. SUZUKI T., ARAI M., MATSUMURA T., ARAI E. *et al*. Factors Associated with Inadequate Tissue Yield in EUS-FNA for Gastric SMT. *ISRN Gastroenterol*., 2011 : 619128.
12. MATSUMOTO H., KOJIMA Y., INOUE T. *et al*. A malignant granular cell tumor of the stomach : Report of a case. *Surg*., 1996, **26** : 119-122.
13. NAGAOKA S., BANDOH T., TOYOHAMA H. A case of malignant granular cell tumor of stomach. *Gastroenterol. Endosc*., 1997, **39** : 1799-1804.
14. FANBURG-SMITH J.C., MEIS-KINDBLOM J.M., FANTE R. *et al*. Malignant granular cell tumor of soft tissue : diagnostic criteria and clinicopathologic correlation. *Am. J. Pathol*., 1998, **22** : 779-794.