

Successful Surgical Treatment of a Recurrent Esophageal Malignant Gastrointestinal Neuroectodermal Tumor

Seung Hwan Song, M.D.¹, Jung Hoon Shin, M.D.¹, Hyang Joo Ryu, M.D.²,
Dae Joon Kim, M.D., Ph.D.¹, Seong Yong Park, M.D., Ph.D.¹

Departments of ¹Thoracic and Cardiovascular Surgery and ²Pathology, Yonsei University College of Medicine

Malignant gastrointestinal neuroectodermal tumor (GNET) is a very rare disease entity, especially in the esophagus. The diagnosis of GNET is based on histologic, immunohistochemical, and genetic findings. The choice of treatment is complete resection, and further treatment options can be considered. Herein, we describe a case of successful surgical treatment of a 23-year-old man with recurrent malignant esophageal GNET.

Key words: 1. Esophageal malignant gastrointestinal neuroectodermal tumor
2. Gastrointestinal neuroectodermal tumor

Case report

A 23-year-old man visited Yonsei University Health System. He had a history of esophageal enucleation surgery and radiotherapy to treat an esophageal malignant gastrointestinal neuroectodermal tumor (GNET) 2 years ago at another hospital. One year after surgery and radiotherapy, the tumor was confirmed to have recurred. Although the doctors recommended surgical resection, the patient hesitated to undergo surgery again, and after another year, the size of the tumor had increased. Eventually he decided to undergo surgical treatment and visited our hospital. Baseline studies such as esophagogastroduodenoscopy (EGD), computed tomography (CT), and positron emission tomography (PET)/CT were performed before the patient consulted us. EGD revealed a mass measuring 2.5×4 cm located 37–41 cm from the upper incisor (Fig. 1A). CT showed a lobulated enhancing mass in the distal esophagus, and PET showed high fluorodeoxyglucose uptake (Fig. 1B, C). The pathologic diagnosis of the mass was re-

current malignant GNET. Immunohistochemical staining was also performed, and the results were positive for SOX-10 and S-100 and negative for P40, synaptophysin, chromogranin, melan-A, and CD-99 (Fig. 2).

The patient underwent the Ivor-Lewis operation. Gastric mobilization was performed through a laparotomy. Via a thoracotomy, the azygous vein and right bronchial artery were divided and an esophagectomy was performed. A wide gastric conduit was tailored, and the anastomosis was made at the level of the azygous vein using a 25-mm end-to-end anastomosis stapler and reinforced with 4-0 Vicryl interrupted sutures. Standard lymph node dissection was performed, and total number of lymph nodes was 45 (5 mid-esophageal, 11 lower esophageal, 8 paracardiac, 10 subcarinal, and 11 left gastric lymph nodes). The pathologic results confirmed the tumor to be an esophageal malignant gastrointestinal tumor. The gross findings of the mass showed an ulcerofungating mass measuring 2.5×4.5 cm. On microscopic examination, the tumor consisted of spindle

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Corresponding author: Seong Yong Park, Department of Thoracic and Cardiovascular Surgery, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea
(Tel) 82-2-2228-2140 (Fax) 82-2-2228-2140 (E-mail) syparkcs@yuhs.ac

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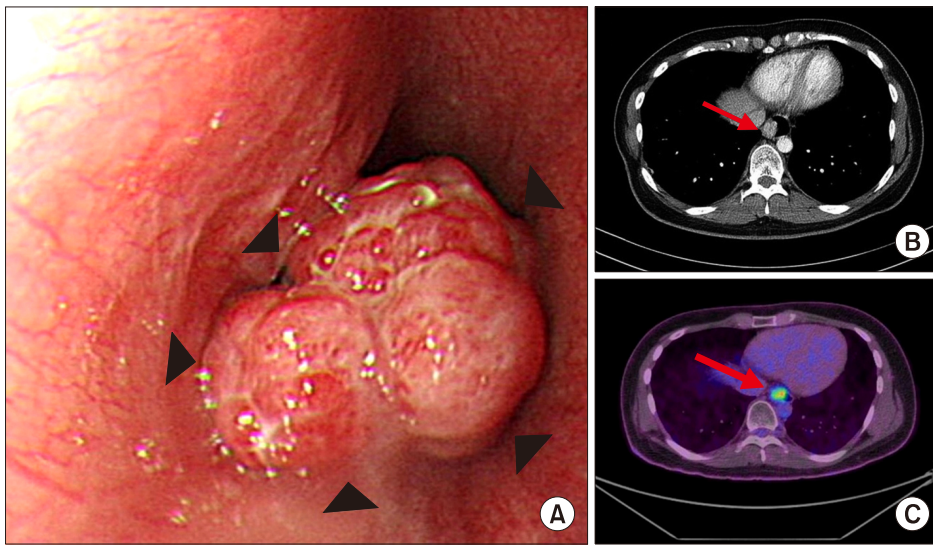


Fig. 1. (A) Preoperative esophagogastroduodenoscopy showed an ulcerofungating mass in the esophagus (arrowhead). (B) A preoperative computed tomography scan showed a mass lesion in the esophagus (arrow), and (C) preoperative positron emission tomography/computed tomography revealed fluorodeoxyglucose uptake by the mass (arrow).

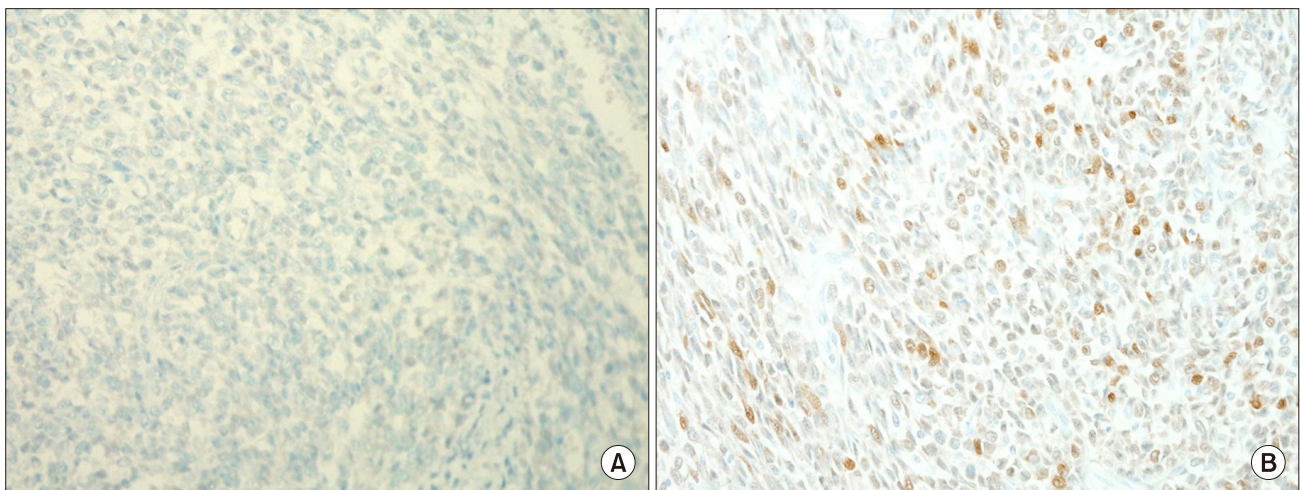


Fig. 2. A histologic examination with immunohistochemical staining showed negativity for melan-A (A) and positivity for S-100 (B) ($\times 200$).

and epithelioid cells, and frequent mitosis was observed, with a mitotic count of 147/50 under a high-power field (Fig. 3). The tumor had invaded into the muscularis propria (pT2), without lymphovascular or perineural invasion, and none of the dissected lymph nodes were involved (pN0). Immunohistochemical staining was performed, and the results were positive for S-100 and negative for melan-A. On the seventh postoperative day, esophagography was performed, showing no leakage or stricture. The patient was gradually moved to a soft diet, and was discharged on the 11th postoperative day. The pathologic results revealed that there was no lymph node metastasis, so we did not consider adjuvant therapy.

Since then, we have been following the patient at our outpatient center and the patient has not shown any evidence of recurrence during the last 2 years.

Discussion

GNET is a rare soft tissue sarcoma, previously described as clear cell sarcoma-like gastrointestinal tumor (CCSLGT) or clear cell sarcoma (CCS) of the gastrointestinal tract. However, GNET is distinct from CCS. Although GNET has some morphological findings that are similar to those of CCS, such as tumor cells with a clear to eosinophilic cytoplasm and a nested growth pattern, there are also subtle differences.

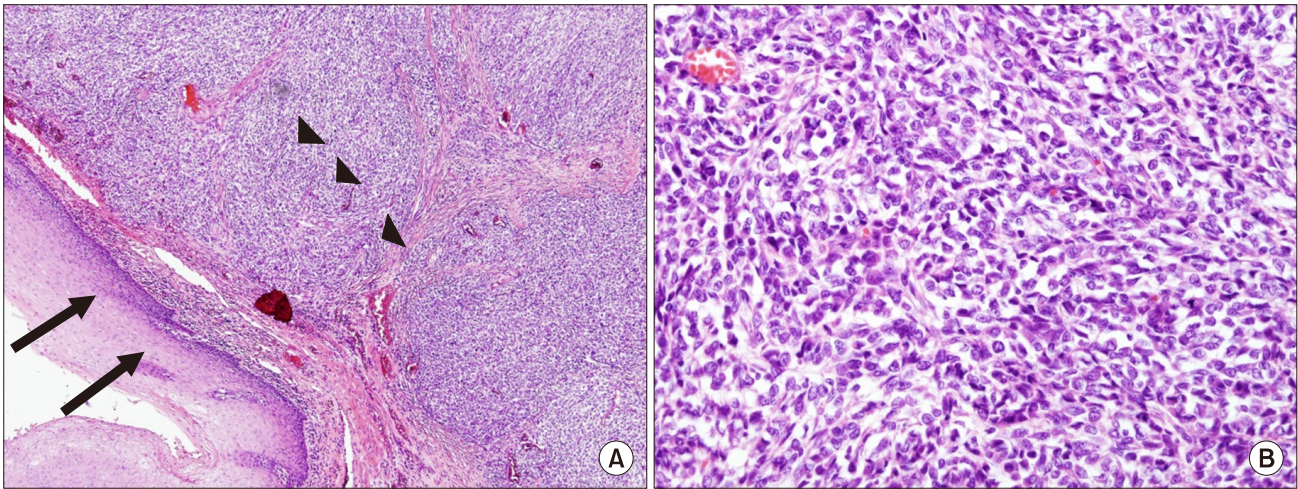


Fig. 3. (A) A histologic examination showed normal esophageal squamous cell epithelium (arrow) and tumor cells (arrowhead) (H&E, $\times 40$), and (B) a tumor consisting of spindle cells with eosinophilic and clear cytoplasm and vesicular nuclei was noted (H&E, $\times 200$).

GNET can be arranged in sheets or nests with epithelioid or oval-to-spindle tumor cells. GNET can show an architecture consisting of pseudoalveolar, pseudopapillary, microcytic, fascicular, cord-like, or rosette-like growth patterns. Moreover, GNET characteristically consists of osteoclast-like giant cells, rather than the wreath-like giant cells in CCS [1-4]. GNET typically shows rearrangements of the *EWSR1* gene, with $t(12;22)(q13;q12)$ *EWSR1-ATF1* or $t(2;22)(q34;q12)$ *EWSR1-CREB1* fusions, which are similar to the genetic findings of CCS [1,5]. Hence, the diagnosis of GNET is based on its histological, immunohistochemical, and genetic features. Stockman et al. [2] described 16 cases of gastrointestinal tumors similar to CCSLGT. CCS usually expresses melanocytic markers such as S-100, melan-A, and human melanoma black (HMB) 45. Unlike CCS, GNET lacks melanocytic differentiation. Further studies revealed that GNET characteristically shows positive results for vimentin, S100, and SOX10, and negative results for HMB 45, melan-A, tyrosinase, CD117, CD34, DOG-1, CD99, α -smooth muscle actin, desmin, and glial fibrillary acidic protein. Therefore, the authors suggested that GNET was a more appropriate name for these tumors [2]. Generally, GNET mainly occurs in young to middle-aged adults, and has a poor prognosis, as it commonly progresses to involve the lymph nodes or metastasizes to the liver [2,6,7].

Chang et al. [8] reported the prevalence and classification of GNET. GNET originates from the cells de-

rived from the neural crest, neuroectoderm, and endoderm. Neuroendocrine tumors have a prevalence of 1.2%–1.5% of all gastrointestinal tumors, with an incidence of 1.6–2.0 new cases per 100,000. Chang et al. [8] reported 187 cases of pathologically proven neuroendocrine tumors involving the gastrointestinal tract. The rectum was the most common location (97 cases, 51.9%). In contrast, the esophagus and small intestine were rare locations (6 cases [3.2%] in the esophagus and 4 cases [2.1%] in the small intestine) [8].

The treatment of choice of GNET is complete surgical resection. However, GNET has aggressive features, with a high rate of recurrence, metastasis, and mortality even after complete resection. Stockman et al. [2] reported that of 12 patients with GNET, 6 died with the tumor, 4 were alive with regional or distant metastasis, and only 2 were alive without recurrence within 41 months. Kong et al. [3] reviewed the literature and reported 40 cases of surgically resected GNET; 5 of these 40 cases had liver metastasis at the initial diagnosis, and 19 cases showed lymph node metastasis. Unfortunately, GNET is a rare disease entity, and information about GNET is lacking, including precise surgical procedures and guidelines regarding the necessity of adjuvant therapy. Therefore, more cases and clinical data are needed in order to understand the behavior of GNET.

Herein, we report the case of a 23-year-old man with a pathologically proven malignant GNET of the

esophagus. The tumor was resected by esophageal enucleation surgery and 1 round of additional radiotherapy was performed. However, the tumor recurred within 2 years. A second round of surgical treatment was performed successfully using the Ivor-Lewis procedure, and the patient has since been healthy, without recurrence.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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