Case of a tumor comprising gastric cancer and duodenal neuroendocrine tumor

Hiroaki Kaneko, Akio Miyake, Yasuaki Ishii, Soichiro Sue, Haruo Miwa, Tomohiko Sasaki, Toshhide Tamura, Masaaki Kondo, Shin Maeda

Department of Gastroenterology, Yokohama City University Graduate School of Medicine, Yokohama 236-0004, Japan

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Correspondence to: Shin Maeda, MD, PhD, Department of Gastroenterology, Yokohama City University Graduate School of Medicine, 3-9 Fukuura Kanazawa-ku, Yokohama 236-0004, Japan. smaeda@yokohama-cu.ac.jp

Telephone: +81-45-7872326
Fax: +81-45-7872327

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Abstract

The present report describes a rare case of a tumor composed of early gastric cancer and a duodenal neuroendocrine tumor (NET). A 78-year-old woman underwent esophagogastroduodenoscopy at a local institution for screening of the upper gastrointestinal tract which revealed a protruded tumor through the pyloric ring from the pyloric antrum. The tumor was too large to treat at the facility; consequently, she was referred to our hospital for further management. Endoscopic submucosal dissection was performed with sufficient free margins in both vertical and horizontal directions. Histopathological findings showed NET confined to the submucosal layer and covered by well-differentiated adenocarcinoma. Immunohistochemical stainings showed that the two lesions existed continuously. While the possibility of a collision cancer was considered, it was suggested that the two lesions existed continuously. Finally, the tumor was diagnosed as gastric cancer composed of duodenal NET G1, with a lymphatic invasion of NET component.

Key words: Gastric cancer; Endoscopic submucosal dissection; Neuroendocrine tumor; Composite-type tumor; Duodenum
A 78-year-old woman presented to a local institution with nausea and right hypochondrial pain. Careful examination led to the diagnosis of gallstones and common bile duct stones. Esophagogastroduodenoscopy (EGD) screening of the upper gastrointestinal tract was performed before surgery to remove the gallstones and a protruded tumor through the pyloric ring from the pyloric antrum was found. Although biopsy specimen from the lesion was diagnosed as an adenoma, the tumor was too large to treat at the facility. The patient was referred to our hospital for further management of the gastric tumor. She had no specific medical history except hypertension and dyslipidemia.

The tumor was resected in a single fashion by the ESD technique, using a GIF-Q260J instrument (Olympus, Tokyo, Japan) with a transparent hood (MAJ-1989-11302; Olympus) attached to the tip of the gastroscope, a dual knife (Olympus), and an insulated tipped knife 2 (Olympus). An electrosurgical current generator (VIO200; ERBE, Tubingen, Germany) was used for the ESD. The tumor was resected with no complications, such as perforation or delayed bleeding. As a result, the patient was discharged on postoperative day 5.

Figure 2 shows a macroscopic view of the resected specimen. The resected mucosa and the tumor measured 54 mm × 40 mm and 38 mm × 32 mm, respectively. The histopathology results showed the resected specimen had sufficient free margins in both vertical and horizontal directions, but the tumor consisted of two components: The first part with irregular atypical epithelium, which formed a tubular and papillary structure confined to the mucosal layer, was a well differentiated adenocarcinoma, and the second part was located near the edge of duodenum side of the specimen and showed a mass composed of nests of small uniform tumor cells, which is typical of NET (Figure 3A-C). These cells were positive for CD56 (Figure 3D), synaptophysin (Figure 3E), and chromogranin A (Figure 3F), and the Ki-67 labeling index was less than 1%. According to the WHO 2010 classification, obvious nuclear fission images were not admitted and finally the NET was diagnosed as G1[3]. The NET cells were detected from the mucosal layer over the submucosa, but no infiltration of the muscle layer was recognized.

The adenocarcinoma cells and the NET cells were in contact. Although migration images were not detected, both component cells had mixed in some parts and formed a tumor duct. Immunohistochemical staining
also showed NET cells coexisting with adenocarcina
coma cells (Figure 3E and F). No venous invasion was
revealed by Elastica van Gieson staining, however,
lymphatic invasion of NET component was seen with
D2-40 staining (Figure 3G).

The patient was sufficiently explained about the
results of the histopathological examination and the
risk of lymph node metastasis; she refused additional
operation and opted for careful observation. Therefore,
close follow-up has been scheduled.

DISCUSSION

Since Oberndorfer proposed the term "carcinoid" in
1907, the origins of NET of the gastrointestinal tract,
as well as the malignancy of these tumors, have
been attracting the attention of clinicians[3]. NETs
are quite rare and almost 55% of NETs occur in the
gastrointestinal tract[2]. In Japan, NET occurs more
frequently in the rectum and the stomach followed by
the duodenum, and primary NET of the duodenum
may occur in less than 5% of all cases[2,4].

Although there were some reports about gastric
collision tumor composed of epithelial and nonepithelial
malignant neoplasm, Morishita et al[5] reported that
a simultaneous incidence of adenocarcinoma and
malignant lymphoma was the most frequent finding
and cases of gastric collision tumor composed of
adenocarcinoma and NET were rare.

Previously, Kato et al[6] reported a case of duodenal

Figure 1  Esophagastroduodenoscopic views of the tumor in the stomach. A: The protruded tumor occupied and existed beyond the pyloric ring, the whole
tumor could not fit in one field of view; B: Image observed by inverting the endoscope in the duodenal bulb; C: Magnifying endoscopy with narrow-band imaging
showed structure irregularities compared with the normal surrounding mucosa.

Figure 2  A macroscopic view of the specimen resected by endoscopic
submucosal dissection. A: Macroscopic appearance of the specimen soaked for
almost 24 h in formalin after endoscopic submucosal dissection. The red dotted
line indicates where there was a pyloric ring; B: Cut out of the resected specimen.
The solid red line indicates adenocarcinoma; green line indicates neuroendocrine
tumor; red dotted line indicates the location of the pylorus.
adenocarcinoma with neuroendocrine features in a 67-year-old woman with acromegaly and thyroid papillary adenocarcinoma. Wen et al.\(^7\) reported a case of duodenal bulb adenocarcinoma with neuroendocrine features in a 63-year-old woman, which was treated by endoscopic mucosal resection. They stated that duodenal adenocarcinoma with neuroendocrine features is extremely rare\(^7\), and as per our review of the published literature, our report is likely the first instance of the gastric adenocarcinoma with duodenal NET resected by endoscopic treatment.

In this report, after ESD, we detected a tiny mass composed of nests of small uniform tumor cells that were typical of NET. The possible reasons the diagnosis of NET was overlooked before ESD are as follows: first, the whole tumor was located over the pylorus and its relatively large size made it difficult to observe the whole tumor precisely; and second, the NET component surface was covered with adenocarcinoma, which was also a protruded lesion.

Collision tumors are thought to arise from morphologically different neighboring neoplasms that do not intermingle\(^8\), but usually, it is not easy to morphologically distinguish a collision-type from a composite-type tumor\(^9\). It was difficult to determine whether the tumor was collision or composite-type in our patient as well: the immunohistochemical staining showed that the two lesions coexisted, suggesting a composite-type tumor, but the NET clinically presented in the duodenal part.

Surgical treatment may have been one treatment adenocarcinoma with neuroendocrine features in a 67-year-old woman with acromegaly and thyroid papillary adenocarcinoma. Wen et al.\(^7\) reported a case of duodenal bulb adenocarcinoma with neuroendocrine features in a 63-year-old woman, which was treated by endoscopic mucosal resection. They stated that duodenal adenocarcinoma with neuroendocrine features is extremely rare\(^7\), and as per our review of the published literature, our report is likely the first instance of the gastric adenocarcinoma with duodenal NET resected by endoscopic treatment.

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Surgical treatment may have been one treatment

**Figure 3** Histopathological results of the resected specimen. A: Low power view of a histological section demonstrates that the neuroendocrine tumor (NET) in the submucosa was covered with adenocarcinoma (HE stain × 40); B: Both component cells had mixed in some parts and formed a tumor alveolar (H&E stain × 400); C: High power view of NET in submucosa (HE stain × 400); D: CD56; E: synaptophysin; F: Chromogranin A staining were positive in the NET cells; G: Lymphatic invasion of the NET component seen with D2-40 staining (× 400).
options, but as the tumor was diagnosed as early gastric cancer which had adaptation for ESD, surgery could be excessively invasive to the patient. By the popularization of ESD, there have been some reports on cancer accompanied by submucosal tumor or NET\[^{5,8,9}\]. However, the coexistence of gastric NET and adenocarcinoma are rare, because gastric neuroendocrine tumors represent less than 1% of all gastric neoplasms\[^{8,10}\]. There have been no previous reports on endoscopic resection of gastric adenocarcinoma with duodenal NET; hence, we considered this case to be extremely rare.

We report the first case of early gastric cancer accompanied by duodenal NET, which was resected by ESD.

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**COMMENTS**

**Case characteristics**

A 78-year-old woman with medical history of hypertension and dyslipidemia presented with a protruded gastric tumor through the pyloric ring from the pyloric antrum.

**Clinical diagnosis**

Magnifying endoscopy with narrow-band imaging showed irregularities in the structures and vessels of the tumor, which the biopsy specimen led to the diagnosis of early gastric cancer.

**Differential diagnosis**

Gastric cancer with submucosal tumor invasion or duodenal cancer.

**Laboratory diagnosis**

All labs were within normal limits.

**Imaging diagnosis**

Computed tomography showed no remarkable metastasis.

**Pathological diagnosis**

A well differentiated adenocarcinoma composed of nests of small uniform tumor cells, which is typical of neuroendocrine tumor (NET).

**Treatment**

Endoscopic submucosal dissection.

**Related reports**

Although there were some reports about gastric collision tumor composed of epithelial and nonepithelial malignant neoplasm, malignant lymphoma was the most frequent finding and cases of gastric collision tumor composed of adenocarcinoma, and NET were rare. Duodenal adenocarcinoma with neuroendocrine features is also extremely rare and there were no previous report on endoscopic resection of gastric adenocarcinoma with duodenal NET.

**Term explanation**

NET is derived from enterochromaffin cells throughout the gastrointestinal (GI), pancreas and bronchopulmonary systems. The most common sites for primary GI carcinoid tumors in Japan are the rectum, stomach, and duodenum.

**Experiences and lessons**

Although we experienced an extremely rare case coincidentally, especially in the case of protruded tumor, the possibilities of collision tumor should be bear in mind.

**Peer-review**

In this paper the authors describe a duodenal neuroendocrine tumor resected by endoscopic submucosal dissection. This is a rare condition and manuscript is well written.

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