Compound gastroenteropancreatic neuroendocrine and gastrointestinal stromal tumors in the stomach: A case report

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Abstract. Gastroenteropancreatic neuroendocrine tumors (GEP-NETs) combined with gastrointestinal stromal tumors (GISTs) are rarely observed in the clinic. In the present study, the case of a 56-year-old female diagnosed with compound GEP-NETs and GISTs was reported. The patient initially presented with epigastric discomfort. The pre-operative diagnosis was of GISTs based on the endoscopic and imaging findings. A subtotal gastrectomy and Roux-en-Y reconstruction were successfully performed. The final diagnosis was revised to be compound GEP-NETs and GISTs based on the pathological findings. After 17 months of follow-up examinations using computed tomography and ultrasonography, the patient showed no symptoms or signs of recurrence.

Introduction

Gastroenteropancreatic neuroendocrine tumors (GEP-NETs) are extremely rare tumors (<1% of stomach tumors) that usually originate from the neuroendocrine tissues of the digestive system. Driver mutations in MEN1, DAXX or ATRX and mTOR pathway genes have been identified as crucial factors in GEP-NETs tumorigenesis (1). The first case of GEP-NETs was reported approximately one century ago. Recently, the incidence of these tumors has greatly increased (2,3). According to the Epidemiology and End Results (SEER) program of the National Cancer Institute, the annual incidence rate of GEP-NETs is 3.65 cases per 100,000 individuals (4). Gastrointestinal stromal tumors (GISTs) are the most common type of mesenchymal tumor of the gastrointestinal system, and are derived from the interstitial Cajal cells of the gastrointestinal tract. GISTs are generally characterized by gain-of-function mutations in the KIT gene (5), and less often by PDGFRA or BRAF gene mutations (6-8). The annual incidence of GISTs ranges between 6.8 and 19.7 individuals per million across numerous countries, including the United States (9-11). GEP-NETs and GISTs are malignant or potentially malignant tumors, and are considered to have their own specific molecular biological behavior. As the majority of patients exhibit nonspecific symptoms, the identification of GEP-NETs and GISTs is often incidental. At present, diagnostic techniques include endoscopy, computed tomography (CT) and endoscopic ultrasonography (EUS) (12) and surgical resection remains the standard treatment for GEP-NETs and GISTs. The present study reports a compound case of GEP-NETs and GISTs that simultaneously occurred in the stomach.

Case report

A 56-year-old female was admitted to the Subei People's Hospital of Jiangsu (Yangzhou, Jiangsu, China) due to epigastric discomfort that had persisted for 4 weeks. Pre-operative blood examinations, including tumor marker analysis, were normal. Gastrointestinal endoscopy identified two fusiform masses of 1.8x1.8 cm and 1.6x1.6 cm located at the gastric body and gastric fundus, respectively (Fig. 1A and B). Meanwhile, EUS found that the two masses with low homogenous echogenicity each originated from the gastric muscular layer (Fig. 2A and B). Additionally, abdominal contrast-enhanced CT confirmed the presence of two well-marginated oval-shaped masses located at the gastric fundus and the lesser curvature of the cardia, respectively (Fig. 3). A pre-operative diagnosis of GISTs was formed.

At laparotomy, the tumor located at the lesser curvature of the cardia was found and measured 3x3x2.5 cm in size. The second tumor was found in the posterior wall of the gastric body and gastric fundus, respectively (Fig. 1A and B). Meanwhile, EUS found that the two masses with low homogenous echogenicity each originated from the gastric muscular layer (Fig. 2A and B). Additionally, abdominal contrast-enhanced CT confirmed the presence of two well-marginated oval-shaped masses located at the gastric fundus and the lesser curvature of the cardia, respectively (Fig. 3). A pre-operative diagnosis of GISTs was formed.

Microscopically, the first tumor was found to be composed of spindle cells, a number of which showed high mitotic activity (Fig.4). Immunohistochemical staining showed that the tumor was positive for (CD)117, CD34, discovered on GIST-1

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ZHOU et al: COMBINED GEP-NETs AND GISTs

and smooth muscle actin (SMA), but negative for desmin and S-100, suggesting a GIST origin.

Unexpectedly, the cells of the second tumor were organized in nests with fibrous separation (Fig. 5). The tumor cells

Figure 1. Pre-operative gastrointestinal endoscopy revealing a mass at the (A) gastric body and (B) the gastric fundus.

Figure 2. Pre-operative endoscopic ultrasonography shows tumors with low homogenous echogenicity originating in the (A) gastric body and (B) the gastric fundus.

Figure 3. Pre-operative abdominal computed tomography demonstrating a single 3.1x2.2-cm mass located close to the gastric fundus and the upper lesser curvature of the stomach.

Figure 4. Hematoxylin and eosin-stained post-operative section. Swirling bundles of spindle cells with focally palisading areas within the fibrotic stroma were identified, but mitotic figures were rare (magnification, x100).

Figure 5. Hematoxylin and eosin-stained post-operative section. Neuroendocrine tumor cells were arranged in nests, with fibrous separation (magnification, x100).
exhibited a mitotic index of <2/10 high-power fields. Immunohistochemical results showed that the tumor was strongly positive for chromogranin A (CgA; +++), synaptophysin (Syn; +++) and CD56 (+++), with a Ki-67 index of <2%. All the results suggested that this tumor was of GEP-NET origin.

Following the surgery, there were no post-operative complications. The patient was discharged from hospital after 10 days. After 17 months of follow-up examinations using CT and ultrasonography, the patient showed no symptoms or signs of recurrence. The present study was approved by the Subei People's Hospital of Jiangsu Ethical Committee and written informed consent was obtained from the patient.

Discussion

GEP-NETs originate from various neuroendocrine tissues of the gastrointestinal system and form the largest subgroup of NETs (13). GEP-NETs usually and equally distribute in the foregut (stomach or duodenal), midgut (jejunal, ileal, appendix or proximal colon) and hindgut (distal colon or rectum) (14). Although they are rare neoplastic diseases in general, the incidence has greatly increased in the last decade (15).

In 2000, the World Health Organization classification system for NETs was published (16). Based on this system, proliferation index (Ki-67, MIB-1), angiogenesis and mitoses are regarded as the most important factors to determine the malignancy of NETs. NETs can be classified into the well-differentiated (<2 cm in size, <2% Ki-67 index, moderately-differentiated (>2 cm in size, >2% Ki-67 index, or angioinvasive) and poorly-differentiated (≥20% Ki-67 index) subtypes (17). In addition, the European Neuroendocrine Tumor Society proposed another grading system (G1, G2 and G3) for the classification of NETs (18). In general, G1 and G2 NETs refer to a well-differentiated subtype, displaying diffuse and intense expression of CgA and Syn. G3 NET indicates a poorly-differentiated subtype with high mitotic counts/Ki-67 index (>20%), displaying slight staining of CgA and intense staining of Syn (19).

GISTs are also rare tumors, but are the most common mesenchymal tumor in the gastrointestinal tract (20). GISTs clinically present with characteristic GI bleeding, weight loss, abdominal pain, anemia and/or a palpable mass (21). The highest incidence of GISTs occurs in the stomach (52-60%), followed by the small intestine (20–30%) and colorectum (10%). Approximately 95% of GISTs are positive for c-KIT/CD117, 40–50% for CD34, 20–30% for SMA (52–60%), followed by the small intestine (20–30%) and their prognostic stratification. Neuroendocrinology 90: 162-166, 2009.


References


