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CASE REPORT

A case of neuroendocrine tumor G1 with unique histopathological growth progress

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Abstract

A gastric neuroendocrine tumor (NET) is generated from deep within the tissue mucosal layers. In many cases, NETs are discovered as submucosal tumor (SMT)-like structures by forming a tumor mass. This case has a clear mucosal demarcation line and developed like a polyp. A dilated blood vessel was found on the surface. The mass lacked the yellow color characteristic of NETs, and a SMT-like form was evident. Therefore, a nonspecific epithelial lesion was suspected and we performed endoscopy with magnifying narrow-band imaging (M-NBI). However, this approach did not lead to the diagnosis, as we diagnosed the lesion as a NET by biopsy examination. The lesion was excised by endoscopic submucosal dissection. The histopathological examination proved that the lesion was a polypoid lesion although it was also a NET because the tumor cells extended upward through the normal gland ducts scatteredly. To our knowledge, there is no previous report of NET G1 with such unique histopathological growth progress and macroscopic appearance shown by detailed examination using endoscopy with M-NBI.

Key words: Neuroendocrine tumor G1; Demarcation line; Polypoid growth; Magnifying narrow-band imaging; Submucosal tumor

Core tip: Neuroendocrine tumors which infiltrate into the mucosa may develop a polypoid appearance mimicking a primary epithelial process.

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INTRODUCTION

Gastric neuroendocrine tumors (NETs) are relatively rare lesions representing approximately 7% of all neuroendocrine tumors and less than 1% of all stomach neoplasms[1]. Most gastric NETs are found incidentally during upper gastrointestinal (GI) endoscopy[2-6]. Gastric NETs usually have the endoscopic appearance of a submucosal tumor because they grow from deep within the mucosal layers and the tumor mass is yellow. The yellow submucosal tumor (SMT) can be detected by white light and the dilated blood vessel on the surface, which is considered to be a secondary change. Gastric NETs comprise 7%

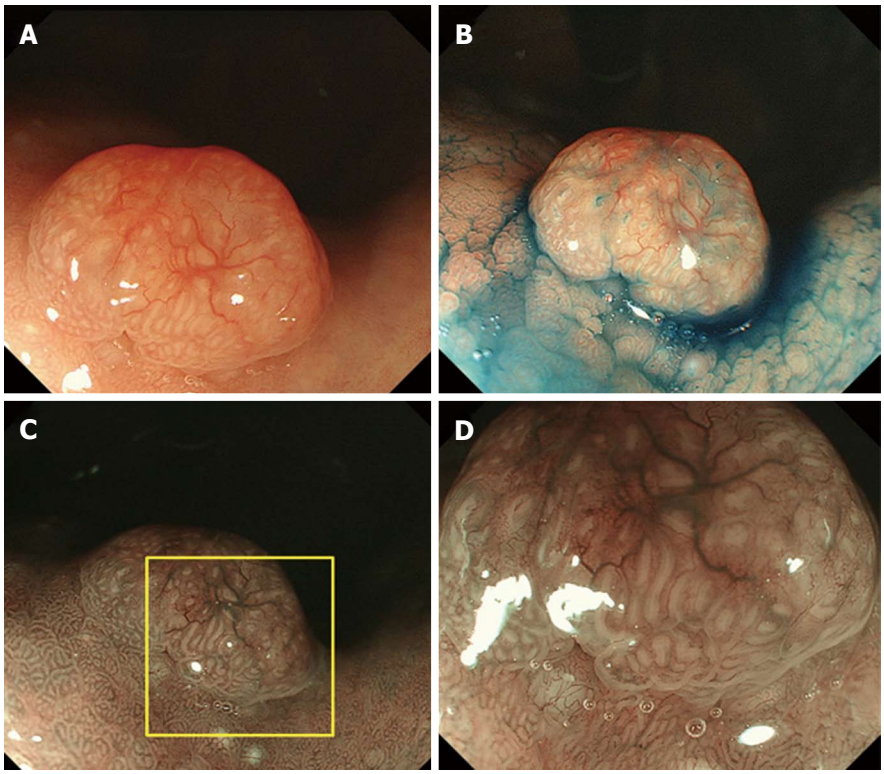

Figure 1 An 8-mm protruded lesion was shown at upper endoscopy. A: Upper endoscopy revealed an 8-mm protruded lesion on the anterior wall of the stomach body. The lesion is the same color as background mucosa and it is not yellow; B: Indigo carmine dye permitted the lesion's demarcation line to become more distinct; C, D: There were dilated vessels on the surface, but neither irregular microvessel patterns nor irregular microsurface patterns were observed by magnifying narrow-band imaging.

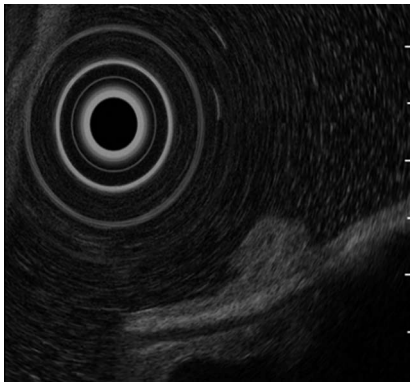

Figure 2 Endoscopic ultrasonography. Endoscopic ultrasonography showed a protruding lesion 8 mm in diameter in the mucosal layer that did not affect the submucosal layer.

of all gastrointestinal NETs and 2% of all excised gastric polyps[7,8]. Randi *et al*[9] classified gastric NETs into three subtypes. Type I NETs typically arise from enterochromaffin-like cell (ECL) hyperplasia, which is stimulated by hypergastrinemia on a background of atrophic gastritis, especially type A gastritis. Type Ⅱ lesions are associated with gastrinomas resulting in Zollinger-Ellison syndrome (ZES). Type Ⅲ lesions are a sporadic disease associated with normal gastrin levels. In type I and Ⅱ diseases, several polyps are often seen in clusters. However, type Ⅲ lesions are usually solitary. The surrounding mucosa may be macroscopically normal, especially in type Ⅲ lesions. Additionally, there may be evidence of atrophy (type I) or associated peptic ulcer (type Ⅱ). Here, we report a case of a type I gastric NET without submucosal tumor shape that extended through the normal gland ducts and developed with polypoid growth.

CASE REPORT

A 61-year-old man presented to his primary care physician with the complaint of mild epigastralgia. An upper GI endoscopy revealed an 8-mm, well-demarcated, protruding lesion on the anterior wall of the stomach body. Therefore, the patient was referred to our hospital. The lesion did not have the reddened appearance of strong inflammation and erosion on the surface like a hyperplastic polyp. The surrounding mucosa was not atrophic. In addition, the lesion was solitary (Figure 1A, B), which contrasts fundic gland polyps that develop as multiple small polyps. Therefore, we performed an endoscopy with magnifying narrow-band imaging (M-NBI) for further evaluation. There were dilated vessels on the surface of the lesion, but there were neither irregular microvessel patterns nor irregular microsurface patterns that indicated neoplastic change under M-NBI (Figure 1C, D). However, the lesion was considered an epithelial neoplasm because the demarcation line was distinct. The pathological evaluation of the biopsy specimen showed the mass was a NET. Endoscopic ultrasonography showed a protruding lesion in the mucosal layer that did not affect the sub-

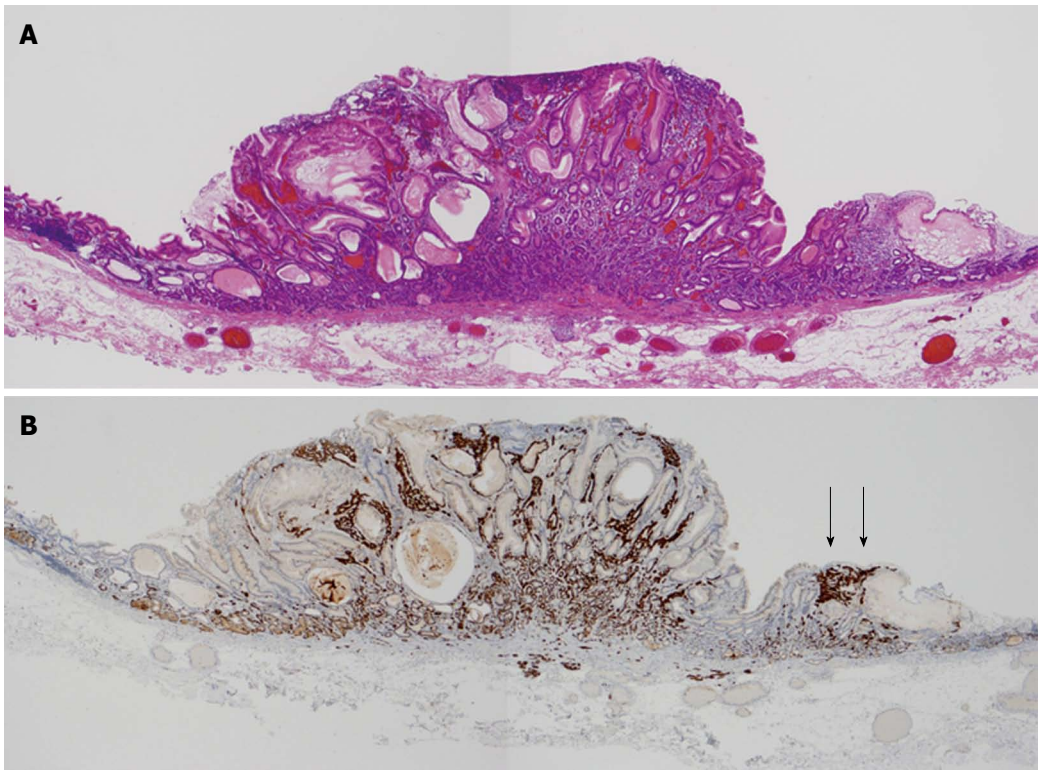

Figure 3 Histological examination of the resected specimen. A: Microscopic examination of the completely resected specimen revealed a neuroendocrine tumor presenting in both the mucosal layer and submucosal layer (hematoxylin and eosin staining); B: Immunohistochemistry for synaptophysin showed that the tumor extended through the normal gland ducts randomly. Enterochromaffin-like cell micro-nests were observed below the normal mucosa (arrow).

mucosal layer (Figure 2).

The laboratory tests revealed normal serum pepsinogen I and serotonin levels, but a markedly increased serum gastrin level (1400 pg/mL; normal range, < 170) and parietal cell antibody level (× 20; normal range, < × 9). The test for anti-Helicobacter pylori IgG was negative. Whole body imaging procedures (CT-scan and abdominal ultrasonography) did not reveal metastatic involvement of any other organ.

We determined the lesion was an atypical gastric NET and conducted endoscopic submucosal dissection. The histopathologic findings of the resected lesion led to the diagnosis of a neuroendocrine tumor of 8 mm × 9 mm. The tumor cells extended through the normal gland ducts scatteredly and infiltrated the submucosal and mucosal layers (Figure 3). Analysis by immunohistochemistry showed positivity for chromogranin A, synaptophysin, and CD56. The Ki-67 proliferation index was 1% (Figure 4). There were numerous ECL hyperplasias and micronests observed under the protruded lesion and in the normal mucosa around the lesion (Figure 3B, yellow arrow). According to the updated Sydney System, intestinal metaplasia was absent. Activity (granulocytic infiltration), inflammation (lymphocytic and mononuclear cell infiltration) and atrophy were moderate at the fornix mucosa and body of the stomach.

As a result of our analysis, we diagnosed the case as a type I neuroendocrine tumor G1 with a very atypical morphological and pathological growth that developed in the background of type A gastritis.

DISCUSSION

Type I NET is the most common lesion type and comprises approximately 70% to 80% of all gastric carcinoids[5,10-12]. According to the World Health Organization's histological classification of gastrointestinal endocrine tumors, a well-differentiated endocrine tumor (synonymous with carcinoid) is defined as an epithelial tumor of usually monomorphous endocrine cells. These tumors have mild or no atypia, grow in the form of solid nests, trabeculae, or pseudoglandular tumors, and are restricted to the mucosa or submucosa[13]. Due to these features, most gastrointestinal NETs have the appearance of submucosal tumors and are visibly yellow by endoscopic examination. However, in the present case, the tumor extended through the normal gland duct scatteredly and did not present a submucosal tumor shape. The result was a well-demarcated polypoid growth presenting like an epithelial neoplasm by endoscopy. The lesion was not yellow and did not present as a tumor except for the mass. Moreover, the lesion did not have the appearance of a hyperplastic polyp and fundic gland polyp.

The percentage of gastric carcinoids amongst all gastric malignancies has increased from 0.3% to 1.77% since the 1950s. The proportion of gastric carcinoids among all gastrointestinal carcinoids has increased from 2.4% to 8.7%[7]. One reason for the increased detection

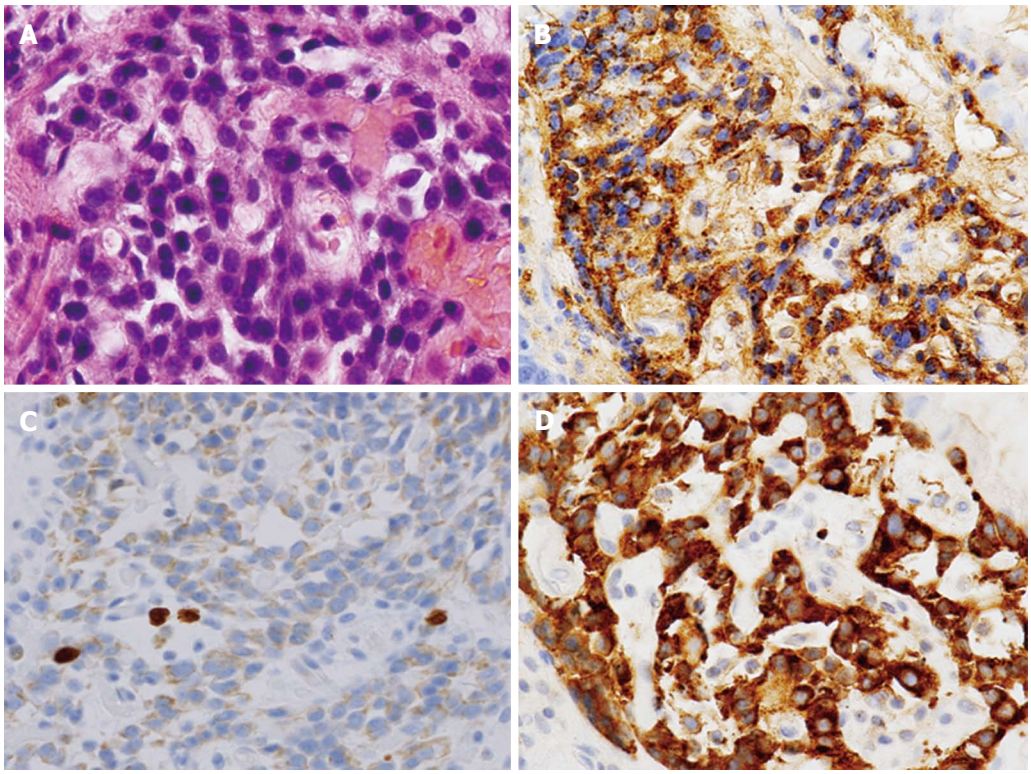

Figure 4 Histological examination of the resected specimen. A: Hematoxylin and eosin staining of the lesion; B: Immunohistochemistry revealed positivity for chromogranin A; C: Only a few positive stained cells were found for Ki-67 and a proliferation index of 1% was evident by immunohistochemistry; D: Immunohistochemistry showed positivity for synaptophysin.

rate is undoubtedly increased awareness of these lesions among pathologists and endoscopists. Additionally, the widespread use of endoscopy and biopsies and the application of immunohistochemical methods have increased detection rates[14]. The increased detection rate has been accompanied by the detection of morphologically and histopathologically untypical lesions. In this report, we present a gastric NET with the unique histopathological growth progress. The lesion did not present as a submucosal tumor but mimicked the endoscopic appearance of epithelial neoplasms.

In the present case, diagnosis by the endoscopic appearance under white light and M-NBI was very difficult. We could not reach a diagnosis until the histopathologic findings of the excised lesion were available. Current methods using M-NBI for the diagnosis of lesions with the endoscopic appearance of typical differentiated adenocarcinoma have been developed and established, especially for the diagnosis of well differentiated adenocarcioma. However, lesions that are confusing and cannot be diagnosed only by endoscopic appearance have been discovered repeatedly. In these cases, biopsies remain necessary. The present case was one such case.

To our knowledge, a NET G1 showing such a macroscopic appearance and histopathological growth progress has not been reported previously. We believe that this is the first report of a NET G1 with such unique histopathological growth progress, including an examination the pathological findings of the excised lesion and the endoscopic appearance under magnifying NBI in detail.

COMMENTS

Case characteristics

A 61-year-old man with the complaint of mild epigastralgia.

Clinical diagnosis

An 8-mm, solitary, well-demarcated, protruding lesion was observed on the anterior wall of the stomach body.

Differential diagnosis

Fundic gland polyp, hyperplastic polyp, adenocarcinoma.

Laboratory diagnosis

A markedly increased serum gastrin level (1400 pg/mL; normal range, < 170) and parietal cell antibody level (× 20; normal range, < × 9); other laboratory tests were within the normal limits.

Imaging diagnosis

Endoscopic ultrasonography showed a protruding lesion in the mucosal layer that did not affect the submucosal layer.

Pathological diagnosis

The biopsy specimen showed the mass was not an epithelial tumor but a neuroendocrine tumors (NETs).

Treatment

The tumor was resected by endoscopic submucosal dissection.

Experiences and lessons

NETs sometimes lack submucosal tumor-like form and mimic epithelial neoplasms if the tumor cells extended through the normal gland ducts scatteredly.

Peer review

NETs which infiltrate into the mucosa may develop a polypoid appearance mimicking a primary epithelial process.

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