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Author contributions: Hayashi K and Kamimura K wrote the manuscript; Hosaka K, Ikarashi S, Kohisa J, Takahashi K, Tominaga K, Mizuno K, Hashimoto S, Yokoyama J, Yamagiwa S, Terai S, Takizawa K and Wakai T diagnosed and treated the patient; Umezu H performed histological analysis; all authors read and approved the final version of the manuscript.

Institutional review board statement: The study was reviewed and approved by the Institutional Review Board of Niigata University.

Informed consent statement: Written informed consent was obtained from the patient for publication of this case report and accompanying images.
performed if accurately diagnosed. Developing a diagnostic methodology including endoscopic ultrasonography (EUS) and fine-needle aspiration (FNA) has allowed us to diagnose the tumor directly through the duodenum. Here, we present a case of a 50-year-old woman with a 27-mm diameter tumor in the pancreatic uncus on computed tomography scan. EUS showed a well-defined hypoechoic mass in the pancreatic uncus that connected to the duodenal proper muscular layer and was followed by endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA). Histological examination showed spindle-shaped tumor cells positively stained for c-kit. Based on these findings, the tumor was finally diagnosed as a duodenal GIST of the extraluminal type, and the patient underwent successful mass resection with partial resection of the duodenum. This case suggests that EUS and EUS-FNA are effective for diagnosing the extraluminal type of duodenal GISTs, which is difficult to differentiate from pancreatic head tumor, and for performing the correct surgical procedure.

**Key words:** Gastrointestinal stromal tumor; Duodenum; Extraluminal type; Pancreatic head tumor; Endoscopic ultrasonography; Endoscopic ultrasound-guided fine-needle aspiration; Partial resection

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**Core tip:** Duodenal gastrointestinal stromal tumors are extremely rare disease entities, and the extraluminal type is difficult to diagnose. Therefore, these tumors have been misdiagnosed as pancreatic tumors; hence, pancreaticoduodenectomy has been performed, although partial duodenectomy can be performed if accurately diagnosed. Recent advances in developing endoscopic ultrasonography and endoscopic ultrasound-guided fine-needle aspiration are helpful for accurate diagnosis of the tumors located in the area and effective for performing the correct surgical procedure.

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**CASE REPORT**

A 50-year-old Japanese woman was found to have a pancreatic head tumor by abdominal ultrasonography on a health checkup and was referred to our hospital for further examination. She was in good physical condition, no evidence of melena, and had no remarkable history. The results of her initial physical examination were as follows: Body temperature, 37.0 °C; blood pressure, 127/78 mmHg; pulse rate, 74 bpm, regular; a flat and soft abdomen without pain or tenderness; and no palpable masses.

Blood tests performed on admission revealed a slight elevated inflammatory response with a white blood cell count of 11370/μL and C-reactive protein level of 0.33 mg/dL. Other laboratory findings were normal including a red blood cell count of 326 × 10^6/μL and hemoglobin of 13.7 g/dL, indicating no existence of anemia. Tumor markers including carbohydrate antigen 19-9, carcinoembryonic antigen, DUPAN, SPan-1, and soluble interleukin-2 receptor levels were within normal limits.

An abdominal dynamic contrast-enhanced computed tomography (CT) showed a 27-mm diameter tumor in the pancreatic uncus, which was well defined and enhanced starting from the arterial to the venous phase, exhibiting the greatest enhancement in the arterial phase (Figure 1). Magnetic resonance imaging revealed the mass to be hypointense on T1-weighted imaging and slightly hyperintense on T2-weighted imaging. The contrast enhancement study showed a similar pattern on CT suggesting the diagnosis of duodenal GIST or pancreatic head neuroendocrine tumor (NET). Therefore, endoscopic examination was performed for the further diagnosis.

Upper gastroendoscopy showed a slightly elevated lesion located in the inferior angle of the duodenum with normal overlying mucosa detected on upper gastrointestinal endoscopy (Figure 2). EUS showed a well-defined hypoechoic mass placed close to the

**INTRODUCTION**

Gastrointestinal stromal tumors (GISTs) are a group of mesenchymal tumors in the gastrointestinal tract that arise from the interstitial cells of Cajal[1]. These tumors contribute to about 1%-3% of all gastrointestinal malignancies and are frequently found in the stomach (60%-70%). Duodenal GISTs are very rare, with 5% rate of occurrence[2]. They are thought to be caused by a mutation in the c-kit gene and alpha-type platelet-derived growth factor receptor gene in the intestinal cells of Cajal or their precursors[3]. Due to its rarity and the complex anatomy of the pancreaticoduodenal region, it is extremely difficult to differentially diagnose duodenal GISTs from pancreatic tumors, especially when it is extraluminal. Because misdiagnosis may lead to an inaccurate choice of surgical procedure, we report our case of extraluminal-type duodenal GISTs correctly diagnosed with endoscopic ultrasonography (EUS) and EUS-guided fine-needle aspiration (EUS-FNA) followed by successful resection of the tumor. To date, the usefulness of these modalities in diagnosing the tumor has not been reported. This case suggests that EUS and EUS-FNA are effective for diagnosing extraluminal type of duodenal GISTs and for performing the correct surgical procedure.
pancreatic uncus; however, the tumor was clearly revealed to be connected to the muscularis propria layer of the duodenum (Figure 3). Based on the EUS findings, duodenal GIST or pancreatic NET was suspected and EUS-FNA was performed for a definitive diagnosis. Histological examination revealed that the tumor was mainly composed of spindle-shaped cells (Figure 4). Immunohistochemistry (IHC) showed that the tumor cells were positive for c-kit, CD34, and S-100, but negative for desmin (Figure 4). Based on these results, the tumor was diagnosed as the extraluminal type of duodenal GIST.

The patient underwent mass resection of the tumor with partial resection of the second part of the duodenum. The tumor showed extraluminal growth and protruded into the pancreas but did not infiltrate the pancreatic parenchyma, consistent with the EUS findings. In addition, there was no ascites and no peritoneal dissemination.

Histopathology of the resected tumor showed a mesenchymal, sharply margined tumor of 30 mm × 22 mm × 22 mm size, consisting of spindle cells without necrosis. Mitosis was detected in 2/50 high-power fields (HPFs). The tumor cells were positive for c-kit, and MIB-1 labeling index (Ki-67 stain) was < 1% (Figure 5).

No postoperative recurrence has been observed to date, and the patient did not require adjuvant chemotherapy for 2 years.

DISCUSSION

GISTs are the most common mesenchymal tumors in the gastrointestinal tract, contributing about 1%-3% of all gastrointestinal malignancies[1]. GISTs develop most

Figure 1  Abdominal dynamic contrast-enhanced computed tomography showed a 27-mm diameter tumor in the pancreatic uncus, which was well defined and enhanced from the arterial phase, exhibiting the greatest enhancement in the arterial phase. White arrow indicates the tumor.

Figure 2  A slightly elevated lesion located in the inferior angle of the duodenum with normal overlying mucosa was detected on upper gastrointestinal endoscopy. White arrows indicate the elevation.

Figure 3  Endoscopic ultrasonography showed a well-defined hypoechoic mass in the pancreatic uncus, and the tumor connected with the muscularis propria layer of the duodenum. Red arrow indicates the tumor and white arrow indicates the muscularis propria layer.

Figure 4  Histological analysis of specimen collected by endoscopic ultrasound-guided fine-needle aspiration. A: Hematoxylin and eosin staining revealed that the tumor was mainly composed of spindle-shaped cells; B: The tumor cells were positive for c-kit.

Figure 5  Histopathology of the resected tumor showed a mesenchymal, sharply margined tumor of 30 mm × 22 mm × 22 mm size, consisting of spindle cells without necrosis. Mitosis was detected in 2/50 high-power fields (HPFs). The tumor cells were positive for c-kit, and MIB-1 labeling index (Ki-67 stain) was < 1% (Figure 5).
frequently in the stomach (60%-70%), followed by the jejunum and ileum (20%-25%), duodenum (5%), colon and rectum (5%), and esophagus (< 5%)\(^3\). Miettinen \textit{et al.}\(^4\) reported that duodenal GISTs most frequently involved the second portion of the duodenum, followed by the third, fourth, and first portions. They also reported that a majority of duodenal GISTs show submucosal tumor with a centrally ulcerated umbilication\(^4\); therefore, duodenal GISTs present with gastrointestinal bleeding, epigastric pain, a palpable mass, and intestinal obstruction\(^4\).

In our case, the tumor exhibited exclusive extraluminal growth into the pancreatic head, and there was a slightly elevated lesion without ulceration in the inferior angle of the duodenum; this atypical finding made it difficult to distinguish it from a pancreatic NET\(^5\). Because the lesion without ulceration is difficult to diagnose by forcep-based biopsy on normal mucosa\(^6\), EUS and EUS-FNA are helpful for its diagnosis. For EUS, it is important to determine whether there is a connection with gastrointestinal wall because it is the most accurate test to distinguish the layer where a lesion is located. The accuracy of the diagnosis was < 50% when using only EUS\(^7\). The sensitivity of EUS-FNA cytology was 84.4% for GISTs located in the stomach but poor for lesions located in the duodenum\(^8\). Table 1 summarizes the cases of duodenal gastrointestinal tumors diagnosed with endoscopic ultrasound-guided fine-needle aspiration. Only a few reports show the usefulness of EUS-FNA for the diagnosis of duodenal GIST, especially when it is extraluminal type. Based on Skandalakis classification, among 11 cases reported, only 3 cases were extraluminal type and 2 showed mixed type. Ueda \textit{et al.}\(^9\) reported that they diagnosed intra- and extraluminal growth type duodenal GIST by EUS-FNA. As summarized, while all case showed somewhat level of submucosal elevation, no ulcer was complicated in the lesion and EUS showed clear hypoechoic mass in nine cases among 11 cases (Table 1). In addition, the connection to the proper muscle layer was shown in nine cases and FNA tissues have successfully performed to determine the histological analyses.

In the reported case, EUS revealed the connection of the tumor and the muscularis propria layer (the fourth EUS layer). EUS-FNA showed that the tumor was composed of spindle-shaped cells, which were positive for c-kit, CD34, and S-100, but not for desmin, reported as a typical IHC result of GIST\(^10\). An accurate diagnosis helped determine the surgical procedure. Therefore, our case was successfully treated as reported\(^11\).

Prognostic factors are very important for both assessing recurrence risk and the choice of adjuvant and neoadjuvant therapy\(^12\). The recently proposed "modified National Institutes of Health (NIH) classification" is defined by four factors: Number, size, location, and rupture of mitoses. This classification may offer advantages in the selection of patients who may require adjuvant therapy\(^13\). All GISTs that occurred in

Figure 5 Histological analysis of resected tumor tissue. A: Macroscopic finding showed 30 mm × 22 mm × 22 mm sized tumor showing extraluminal growth from duodenum (black arrow); B: Hematoxylin and eosin-stained sections showed that the tumor was mainly composed of spindle-shaped cells without necrosis; C: The tumor cells appeared immunohistochemically positive for c-kit; D: Mitosis was detected in 2/50 high-power fields, and MIB-1 labeling index (Ki-67 stain) was < 1%.
the intestines had more than a moderate possibility of metastasis when they were > 5 cm or had > 5 mitoses/50 HPFs. In tumors < 5 cm with a mitotic count < 5/50 HPFs, the intestinal GISTs had a low probability of metastasis [14].

Patients with duodenal GISTs classified as intermediate or high risk for tumor relapse should be treated with 400 mg imatinib daily for 3 years and there is no benefit for patients classified at low risk. As summarized in Table 1, other than 2 cases with no follow up data are available after the surgical treatment, no recurrence after the surgical treatment was confirmed in all other 6 cases for whom the surgery was performed. While other 3 cases showed stable disease with no surgical treatment because of low risk. Our patient was low risk according to the NIH consensus criteria for risk satisfaction of GISTs and has been followed without adjuvant chemotherapy.

After completed tumor resection, follow-up care should be every 3-6 mo, including clinical examination and CT scans of the abdomen and pelvis once a year for 5 years [15]. Our patient has been doing well with no tumor recurrence for 2 years since her surgery and will continue strict CT follow-up.

In summary, we have described a rare extraluminal growth type of duodenal GIST and showed the usefulness of EUS-FNA. This report will aid physicians in diagnosing rare duodenal tumors and contribute to determining the appropriate therapeutic strategy.

### Table 1  Summary of cases of duodenal gastrointestinal tumors diagnosed with endoscopic ultrasound-guided fine-needle aspiration

| Ref. | Age (yr) | Gender | Location in duodenum | Size (mm) | Endoscopic finding | EUS finding | Immunohistochemistry | Clinical course | Treatment | Adjuvant chemotherapy | Follow up period (yr) | Pathological characteristics |
|------|----------|--------|----------------------|----------|-------------------|-------------|----------------------|-----------------|-----------|----------------------|--------------------------|-----------------------------|
| 9    | 72       | F      | Central depression   | 26±      | hypo              | +            | +                    | +               | Partial duodenectomy | No recurrence          | N.A                         |
| 16   | 62       | M      | Ulcerative lesion    | 40±      | hypoe             | +            | +                    | +               | Partial duodenectomy | No recurrence          | N.A                         |
| 17   | 69       | F      | Well-delineated      | 35±      | hypoe             | +            | +                    | +               | Partial duodenectomy | No recurrence          | N.A                         |
| 18   | 76±      | M      | Cystic change        | 35±      | hypoe             | +            | +                    | +               | Partial duodenectomy | No recurrence          | N.A                         |
| 19   | 76±      | M      | Connected to proper muscles | 20±      | hypoe             | +            | +                    | +               | Partial duodenectomy | No recurrence          | N.A                         |
| 21   | 31±      | M      | Internal echogram    | 30±      | hypoe             | +            | +                    | +               | Surgery (no detail available) | No recurrence          | N.A                         |
| 20   | 75±      | M      | Central depression   | 60±      | hypoe             | +            | +                    | +               | Partial duodenectomy | No recurrence          | N.A                         |
| 21   | 51±      | M      | Ulcerative lesion    | 275±     | hypoe             | +            | +                    | +               | Partial duodenectomy | No recurrence          | N.A                         |
| 21   | 30±      | M      | Ulcerative lesion    | 30±      | hypoe             | +            | +                    | +               | Partial duodenectomy | No recurrence          | N.A                         |
| 21   | 50s      | F      | Central depression   | 30±      | hypoe             | +            | +                    | +               | Partial duodenectomy | No recurrence          | N.A                         |
| 21   | 85±      | F      | Central depression   | 30±      | hypoe             | ±            | +                    | ±               | Partial duodenectomy | No recurrence          | N.A                         |
| 21   | 50s      | F      | Central depression   | 30±      | hypoe             | ±            | +                    | ±               | Partial duodenectomy | No recurrence          | N.A                         |
| 21   | 30±      | F      | Central depression   | 30±      | hypoe             | ±            | +                    | ±               | Partial duodenectomy | No recurrence          | N.A                         |
| 21   | 50s      | F      | Central depression   | 30±      | hypoe             | ±            | +                    | ±               | Partial duodenectomy | No recurrence          | N.A                         |

EUS: Endoscopic ultrasound; ALT: Alanine aminotransferase.

Hayashi K et al. EUS-FNA for extraluminal duodenal GIST
Clinical diagnosis
A mass in the pancreatic uncus that connected to the duodenal proper muscular layer.

Differential diagnosis
Pancreatic cancer; gastrointestinal stromal tumors; neuroendocrine tumor.

Laboratory diagnosis
Laboratory data showed a slight elevated inflammatory response with a white blood cell count of 11370/μL and C-reactive protein level of 0.33 mg/dL. Tumor markers including carbohydrate antigen 19-9, carcinoembryonic antigen, DUPAN, SPan-1, and soluble interleukin-2 receptor levels were within normal limits.

Imaging diagnosis
EUS showed a well-defined hypoechoic mass in the pancreatic uncus that connected to the duodenal proper muscular layer. Magnetic resonance imaging revealed the mass to be hypointense on T1-weighted imaging and slightly hyperintense on T2-weighted imaging. The imaging studies suggested the diagnosis of duodenal GIST or pancreatic head neuroendocrine tumor (NET).

Pathological diagnosis
IHC showed that the tumor cells were positive for c-kit, CD34, and S-100, but negative for desmin. Based on these results, the tumor was diagnosed as the gastrointestinal stromal tumor.

Treatment
The patient underwent successful mass resection with partial resection of the duodenum.

Term explanation
GISTs: Gastrointestinal stromal tumors; NET: Neuroendocrine tumor; EUS: Endoscopic ultrasonography; FNA: Fine-needle aspiration.

Experiences and lessons
This case suggests that EUS and EUS-FNA are effective for diagnosing the extraluminal duodenal GIST.

Peer-review
This is a well written case.

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P- Reviewer: Huang CM, Yang F S- Editor: Gong ZM
L- Editor: A E- Editor: Lu YJ
