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The Selective Arterial Calcium Injection Test is a Valid Diagnostic Method for Invisible Gastrinoma with Duodenal Ulcer Stenosis: A Case Report

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ABSTRACT

The localization and diagnosis of microgastrinomas in a patient with multiple endocrine neoplasia type 1 is difficult preoperatively. The selective arterial calcium injection (SACI) test is a valid diagnostic method for the preoperative diagnosis of these invisible microgastrinomas. We report a rare case of multiple invisible duodenal microgastrinomas with severe duodenal stenosis diagnosed preoperatively by using the SACI test. A 50-year-old man was admitted to our hospital with recurrent duodenal ulcers. His serum gastrin level was elevated to 730 pg/ml. It was impossible for gastrointestinal endoscopy to pass through to visualize the inferior part of the duodenum, because recurrent duodenal ulcers had resulted in severe duodenal stenosis. The duodenal stenosis also prevented additional endoscopic examinations such as endoscopic ultrasonography. Computed tomography did not show any tumors in the duodenum and pancreas. The SACI test provided the evidence for a gastrinoma in the vascular territory of the inferior pancreaticoduodenal artery. We diagnosed a gastrinoma in the peri-ampullary lesion, so we performed Subtotal Stomach-Preserving Pancreaticoduodenectomy with regional lymphadenectomy. Histopathological findings showed multiple duodenal gastrinomas with lymph node metastasis and nonfunctioning pancreatic neuroendocrine tumors. Twenty months after surgery, the patient is alive with no evidence of recurrence and a normal gastrin level. In conclusion, the SACI test can enhance the accuracy of preoperative localization and diagnosis of invisible microgastrinomas, especially in the setting of severe duodenal stenosis.

Key words: *Selective arterial calcium injection test, Gastrinoma, Duodenal stenosis, Multiple endocrine neoplasia type 1*

Gastrinoma is the most common neuroendocrine tumor in patients with multiple endocrine neoplasia type 1 (MEN 1)^{6,10,11}. Gastrinomas in a patient with MEN 1 tend to be multiple and too small for imaging methods to show them, making the localization and diagnosis of these microgastrinomas difficult preoperatively. Endoscopic ultrasonography (EUS) is a useful method for showing and diagnosing submucosal microgastrinomas, but in a case of severe stenosis caused by recurrent ulcers, it was impossible for EUS to pass through the stenosis and show the microgastrinomas. Some have recommended the use of the selective arterial calcium injection (SACI) test as a valid diagnostic

method for the localization of these invisible microgastrinomas preoperatively^{4,8,12}. We report a rare case of multiple invisible duodenal microgastrinomas and pancreatic neuroendocrine tumors in a patient with MEN 1 with severe duodenal stenosis diagnosed preoperatively by using the SACI test.

CASE PRESENTATION

A 50-year-old man was admitted to our hospital with recurrent duodenal ulcers causing epigastric pain, nausea and vomiting. He had been treated with proton pump inhibitors for duodenal ulcers for 2 years. Despite continuous proton pump

List of abbreviations SACI: Selective arterial calcium injection, MEN 1: Multiple endocrine neoplasm type 1
EUS: Endoscopic ultrasonography, GIS: Gastrointestinal endoscopy, CT: Computed tomography
IPDA: Inferior pancreaticoduodenal artery, MRI: Magnetic resonance imaging
SSPPD: Subtotal Stomach-Preserving Pancreaticoduodenectomy, DNETs: Duodenal neuroendocrine tumors
PNETs: Pancreatic neuroendocrine tumors, CgA: Chromogranin A

inhibitor treatment, his abdominal symptoms did not improve. There was no other past medical history except for the duodenal ulcers. His father had died of an unspecified pancreatic tumor. Laboratory tests showed elevated levels of serum calcium (12.8 mg/dl), gastrin (730 pg/ml), and parathyroid hormone (2,000 pg/ml), but prolactin was normal (18.3 ng/ml).

Gastrointestinal endoscopy (GIS) showed a giant ulcer filling one third of the lumen of the duodenum. It was impossible to pass the endoscope through this lesion to view the inferior part, because recurrent duodenal ulcers had resulted in severe duodenal stenosis. In addition, the duodenal stenosis prevented additional endoscopic examinations such as EUS from showing submucosal tumors such as gastrinomas and obtaining specimens by fine-needle aspiration of the tumors. The tissue biopsied from these ulcerative lesions was negative for duodenal carcinoma. Contrast-enhanced computed tomography (CT) showed duodenal wall thickening and edema of the descending part of the duodenum, but did not show tumors in the duodenum and pancreas (Fig. 1a). Only one lymph node sized within 16 mm in diameter in the posterior part of the head of pancreas was enhanced (Fig. 1b). Angiography and the SACI test were performed to identify the arterial supply of the gastrinoma. The gastroduodenal artery, inferior pancreaticoduodenal artery (IPDA), proper hepatic artery and splenic artery were selectively catheterized. This test provided the evidence for a gastrinoma in the vascular territory of the IPDA, the peri-ampullary lesion, and the absence of hepatic metastases (Fig. 2). In addition, parathyroid and pituitary gland evaluation were conducted to diagnose the MEN 1. Thyroid ultrasonography showed a suspected

parathyroid adenoma, but brain magnetic resonance imaging (MRI) showed a normal pituitary gland.

We diagnosed a gastrinoma in the peri-ampullary lesion with MEN 1, so we performed Subtotal Stomach-Preserving Pancreaticoduodenectomy (SSPPD) with regional lymphadenectomy (Fig. 3).

Histopathological findings showed 4 small neuroendocrine tumors sized within 3 mm in the duodenum (DNETs) (Fig. 4a-c), 4 small neuroendocrine tumors sized within 3mm in the head of pancreas (PNETs) (Fig. 5a-c) and 1 lymph node metastasis in the posterior part of the head of pancreas (Fig. 6a-b). Immunohistochemical examination found that the DNETs and the lymph node metastasis were positive for chromogranin A (CgA), synaptophysin and gastrin. On the other hand, the PNETs were positive for CgA and synaptophysin, but negative for gastrin. The Ki-67 labeling index of the DNETs and the metastatic lymph node were about 10%, and that of the PNETs was < 2%. By WHO classification 2010, the DNETs were NET G2, and the PNETs were NET G1. The patient was diagnosed with multiple duodenal gastrinomas with lymph node metastasis and nonfunctioning PNETs with MEN 1.

In the postoperative course, the pancreatic fistula as a complication was treated with conservative measures. He was discharged from the hospital on the 51st postoperative day. Ten months after the surgery, parathyroidectomy was performed for the suspected parathyroid adenoma. Histopathological findings showed the parathyroid adenoma. Now twenty months after the first surgery, SSPPD, the patient is alive with a normal gastrin level and without any evidence of recurrence.

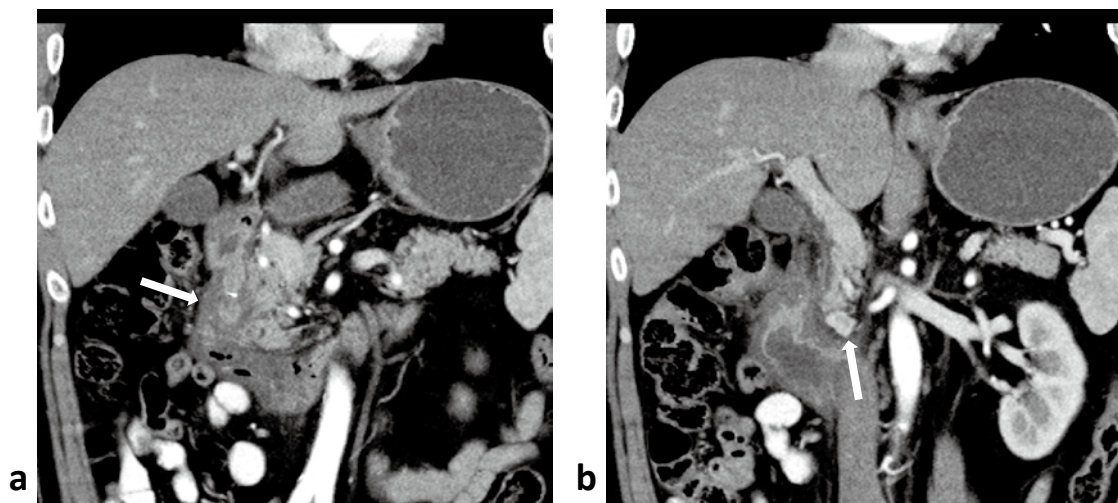


Fig. 1. Computed tomography.

(a) Arrow indicates duodenal wall thickening and edema.

(b) Arrow indicates enhanced lymph node sized within 16 mm in diameter in the posterior part of the head of pancreas.

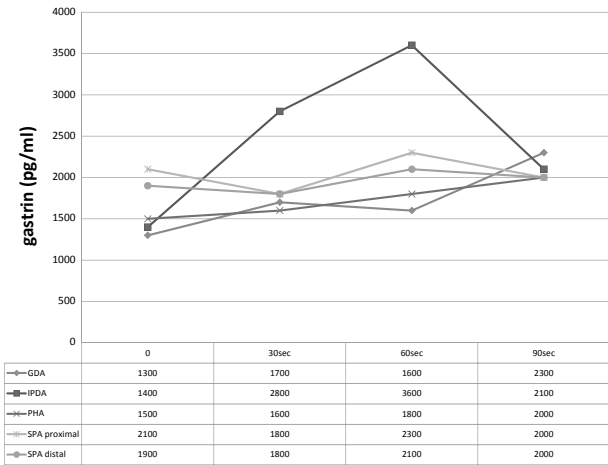


Fig. 2. Results of the SACI test. The gastroduodenal artery, inferior pancreaticoduodenal artery (IPDA), proper hepatic artery and splenic artery were selected. Injection of calcium into IPDA resulted in a sharp rise in this artery gastrin levels (before: 1400 pg/ml, after 60s: 3600 pg/ml).



Fig. 3. We performed Subtotal Stomach-Preserving Pancreaticoduodenectomy with regional lymphadenectomy.

Histopathological findings of the resected specimen.

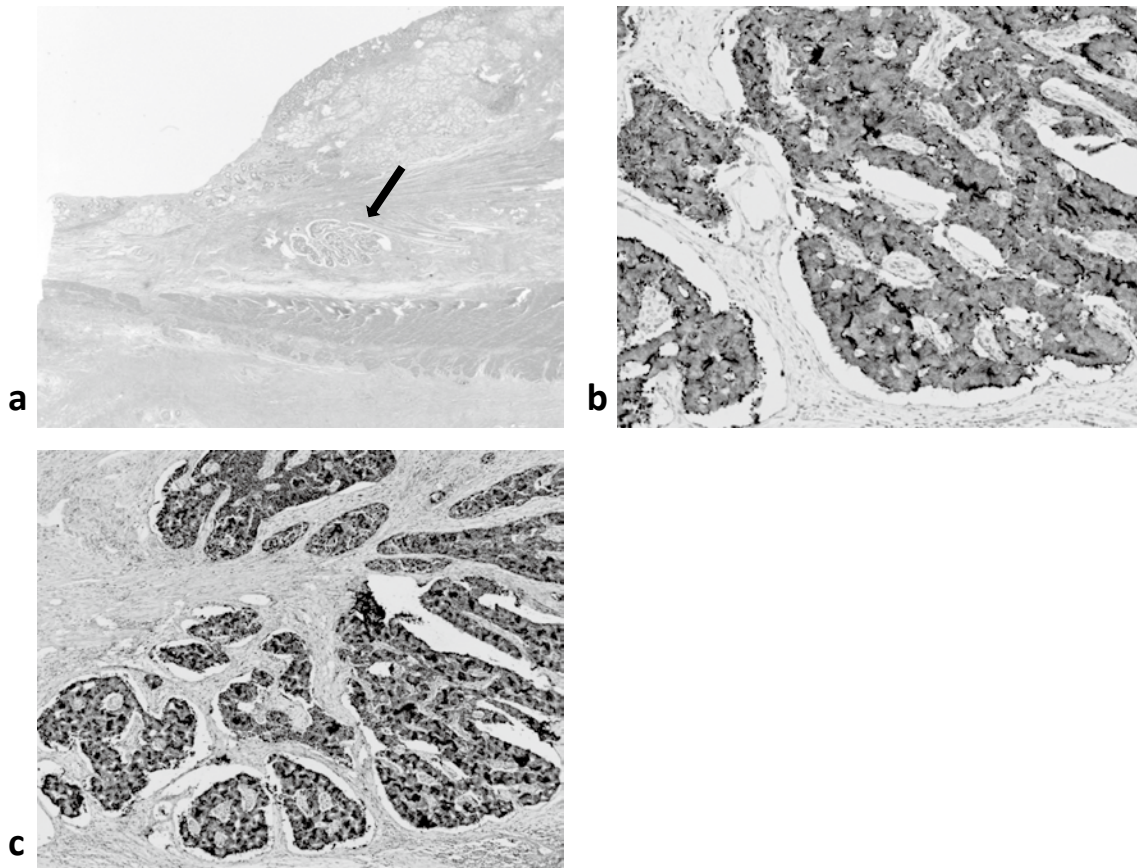


Fig. 4. Small duodenal neuroendocrine tumors. (a) H.E staining. Arrow indicates one of 4 small submucosal tumors sized within 3 mm. (b) Immunohistochemical staining for CgA. The tumors were positive for CgA. They were duodenal neuroendocrine tumors (DNETs). (c) Immunohistochemical staining for gastrin. The DNETs were positive for gastrin. They were diagnosed as duodenal gastrinomas.

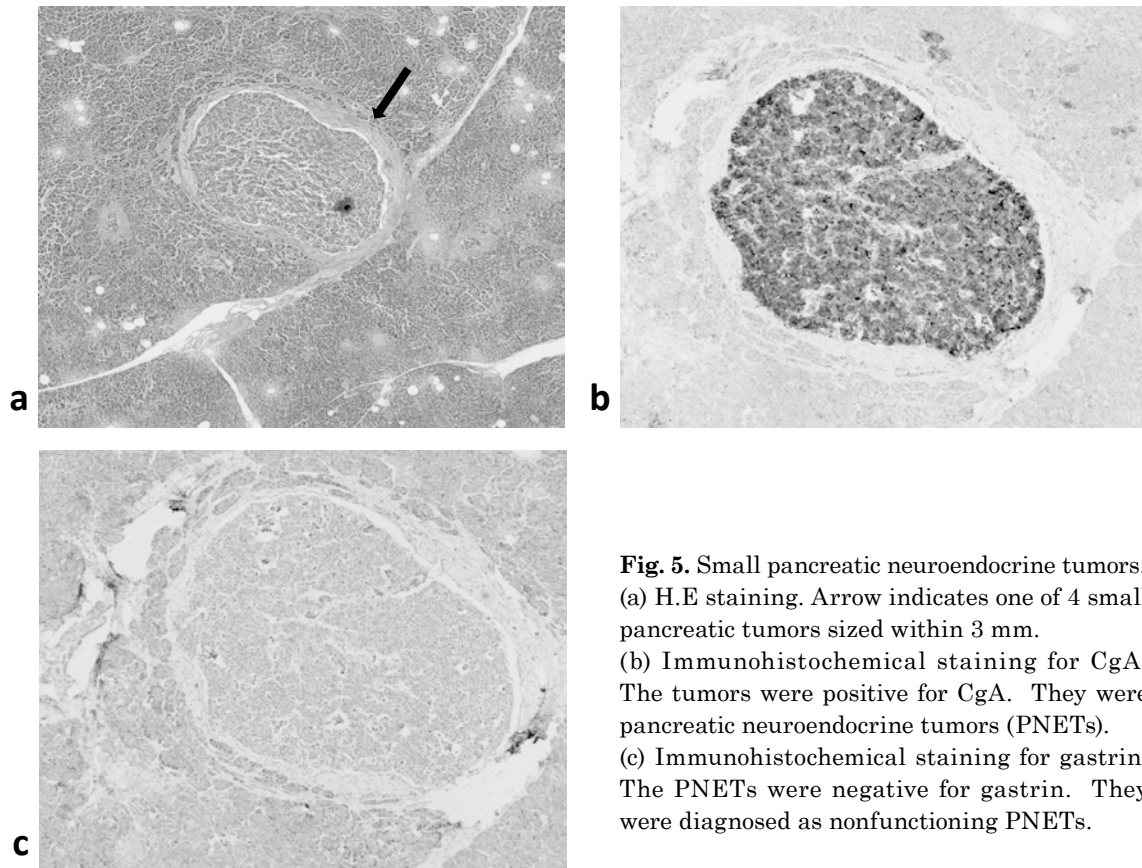


Fig. 5. Small pancreatic neuroendocrine tumors. (a) H.E staining. Arrow indicates one of 4 small pancreatic tumors sized within 3 mm. (b) Immunohistochemical staining for CgA. The tumors were positive for CgA. They were pancreatic neuroendocrine tumors (PNETs). (c) Immunohistochemical staining for gastrin. The PNETs were negative for gastrin. They were diagnosed as nonfunctioning PNETs.

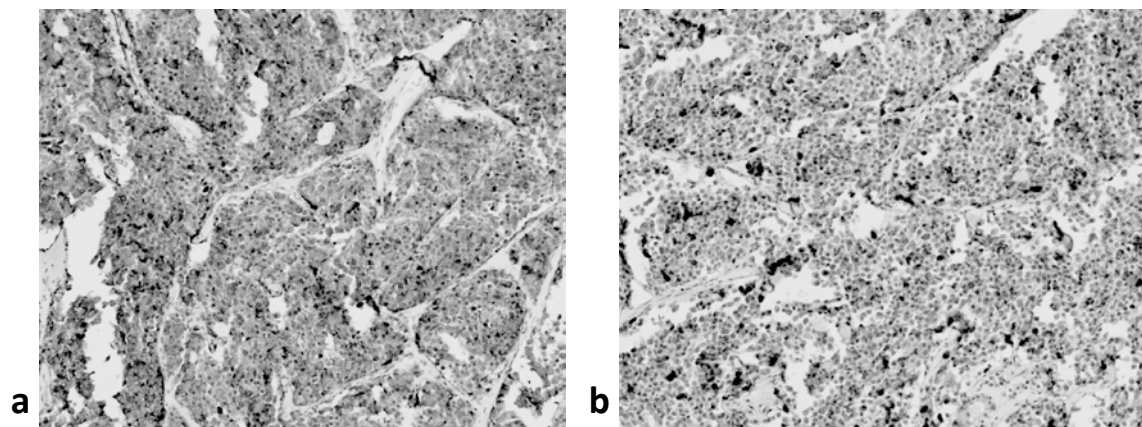


Fig. 6. The metastatic lymph node.

- (a) Immunohistochemical staining for CgA. The lymph node was positive for CgA. It was metastatic lymph node of NETs.
 (b) Immunohistochemical staining for gastrin. The metastatic lymph node was positive for gastrin. It was diagnosed as the metastatic lymph node of duodenal gastrinomas.

DISCUSSION

The SACI test is a highly accurate and safe method for the preoperative localization and diagnosis of gastrinomas with MEN 1 in the duodenum or/and pancreas and is especially helpful in a case of duodenal stenosis. More than half of duodenal gastrinomas with MEN 1 tend to be smaller than 1 cm in diameter^{3,12}. Imaging studies such as GIS,

contrast-enhanced CT, and MRI are used for preoperative diagnosis of microgastrinomas, but these imaging studies may fail to show them. EUS is also a useful method for detecting submucosal small tumors as small as 2-3 mm in diameter¹ but, in our case, severe duodenal stenosis prevented careful examination with any standard modality. The SACI test was the only valid method for localization and diagnosis of the invisible microgastrino-

mas.

The treatment strategy for gastrinomas with MEN 1 has been controversial. We recommend early and aggressive surgical resection of gastrinomas, because recently published articles suggest that this improves survival rates and the long term biomedical cure of gastrinomas as well as decreasing the rate of hepatic metastases^{2,5,7,9}. The preoperative diagnosis in our case was invisible gastrinomas in the peri-ampullary lesion, so we selected “total” duodenectomy rather than “partial” duodenectomy. In addition, any regional lymph nodes around the head of the pancreas and hepatic artery should be dissected, because duodenal gastrinomas reportedly metastasize to regional lymph nodes independent of size^{7,8}. In our case, the preoperative CT showed one highly enhanced lymph node sized within 16 mm in diameter in the posterior part of the head of the pancreas. Pancreas preserving total duodenectomy to save the head of the pancreas offered a less invasive surgery compared with SSPPD, but this procedure did not allow for regional lymph node dissection and the resection of microgastrinomas in the head of the pancreas. With total duodenectomy, regional lymph node dissection and the possibility of microgastrinomas in the head of pancreas, we performed SSPPD. As a result, pathological findings showed that one highly enhanced metastatic lymph node was larger than the primary duodenal microgastrinomas, so it was possible for the metastatic lymph node to secrete more gastrin than the duodenal microgastrinomas and to be fed from IPDA, identified by the SACI test as the arterial supply of the gastrinoma. Proper preoperative diagnosis by the SACI test and early and aggressive surgical resection contributed to curative R0 resection and recurrence-free survival.

CONCLUSION

The SACI test can enhance the accuracy of preoperative localization and diagnosis of invisible microgastrinomas, especially in the setting of severe duodenal stenosis.

Consent

Written informed consent was obtained from the patient for publication of this Case Report and any accompanying images.

Competing interests

The authors declare that they have no competing interests.

Authors' contribution

TS conceived of this case presentation and drafted the presentation. KM, YY, YS, YH, HK, HO and TS participated in the design of this case presentation. FS carried out the pathological

studies. All authors read and approved the final manuscript.

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