Case Report

Case of primary hepatic gastrinoma: Diagnostic usefulness of the selective arterial calcium injection test

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INTRODUCTION

Gastrinomas usually occur in the duodenum and pancreas. Primary hepatic gastrinoma is rare and difficult to diagnose because the liver is a frequent site of metastatic gastrinomas. Clinical factors were assessed in a 28-year-old man with diarrhea and heartburn who was hospitalized for recurrent duodenal ulcers. Abdominal ultrasound, endoscopic ultrasound and computed tomography (CT) could not detect a tumor in the duodenum or pancreas. His gastrin level was 846 pg/mL and magnetic resonance imaging showed a mass 12 mm in diameter in the right robe of the liver. A selective intra-arterial calcium injection (SACI) test and 68-gallium edotreotide positron emission tomography CT (Ga-DOTATOC PET-CT) were therefore performed. Calcium gluconate injection into the proper hepatic artery resulted in a marked increase in serum gastrin concentration in the right hepatic vein, with Ga-DOTATOC PET-CT showing uptake only by the liver mass. Following a diagnosis of primary hepatic gastrinoma, the tumor was resected. A histopathological examination indicated gastrinoma. Six months postoperatively, he has no symptoms, is not taking proton-pump inhibitors and his gastrin level remains within the normal range. The SACI test and the clinical course of this patient strongly suggest that the tumor was a primary hepatic gastrinoma. The SACI test is helpful in the diagnosis of primary hepatic gastrinoma.

Key words: gastrinoma, liver, selective arterial calcium injection test, Zollinger–Ellison syndrome

CASE REPORT

A 28-YEAR-OLD MAN was admitted to our hospital in January 2012 because of a bleeding gastric ulcer. He was treated with endoscopic ablation and administration of proton-pump inhibitors (PPI). He was positive for the antibody against Helicobacter pylori, necessitating antibiotic treatment. Following H. pylori eradication, he stopped taking PPI, but he was hospitalized for recurrent duodenal ulcer and placed back on PPI. His serum gastrin concentration was 846 pg/mL (normal range, 37–172), suggesting a gastrinoma. Abdominal ultrasound and computed tomography (CT) showed no tumors in the pancreas or duodenum. But he again had diarrhea and heartburn whenever he stopped taking PPI. Magnetic resonance imaging (MRI) performed in April 2013 showed a mass measuring 12 mm in diameter in the right robe of the liver (Fig. 1a). Endoscopic ultrasound performed to localize a possible gastrinoma in the gastrinoma triangle was unable
to identify any tumors. We therefore performed a SACI test to detect the site of the possible gastrinoma (Fig. 1b). Hepatic mass showed abundant blood flow. The superior mesenteric artery, splenic artery, gastroduodenal artery and proper hepatic artery were selectively catheterized by the rapid injection of calcium gluconate. Blood samples were obtained through the catheter from the right or left hepatic vein before and 20, 40, 60, 90 and 120 s after calcium injection. Serum gastrin concentration in blood taken from the right hepatic vein was markedly elevated 20 s after calcium gluconate injection into the proper hepatic artery. In contrast, calcium gluconate injection into the other arteries had no effect on serum gastrin concentration (Fig. 2). A 68-gallium edotreotide positron emission tomography CT (Ga-DOTATOC PET-CT) scan showed uptake only by the liver mass (Fig. 3), resulting in a diagnosis of primary hepatic gastrinoma.

Brain MRI and thyroid ultrasound were performed to exclude multiple endocrine neoplasia type 1 syndrome (MEN-1), but there were no abnormalities in the pituitary or parathyroid glands. Moreover, the serum

Figure 1  (a) T2-weighted magnetic resonance imaging showing a mass (arrow) in right robe of the liver. (b) Angiography of the celiac artery in our patient showing a tumor (arrow) in the right robe of the liver.

Figure 2  Results of selective intra-arterial calcium injection tests showing serum gastrin concentrations as a function of time after calcium injection. — superior mesenteric artery–right hepatic vein; —— distal splenic artery–right hepatic vein; ——- proximal splenic artery–right hepatic vein; ——- gastroduodenal artery–right hepatic vein; ——- proper hepatic artery–right hepatic vein; ——- left hepatic artery–left hepatic vein.

Figure 3  68-Gallium edotreotide positron emission tomography computed tomography result, showing uptake by a mass (arrow). (a) Fusion image. (b) Maximum intensity projection image.
concentrations of calcium, phosphorous, prolactin and parathyroid hormone were normal.

The tumor was subsequently resected, with a histopathological examination indicating that the mass was a gastrinoma (Fig. 4). Six months postoperatively, he has no symptoms, is no longer taking PPI and his serum gastrin level remains within normal range.

DISCUSSION

ZOLLINGER–ELLISON SYNDROME (ZES) is caused by malignant gastrin-producing neuroendocrine tumors, called gastrinomas. Although ZES is generally sporadic, ZES is part of MEN-1 in approximately 20–30% of patients.¹

Generally, gastrinomas are localized in the gastrinoma triangle. Only 5.6% of gastrinomas are located outside this area,² with primary hepatic gastrinomas being very rare. Patients with primary hepatic gastrinomas are slightly younger than patients with gastrinomas in the gastrinoma triangle.³ They are reportedly more common in men than in women, and they have not been associated with MEN-1.⁴ The results in our patient were compatible with these characteristics.

Pancreatic gastrinomas tend to be relatively large, with a reported mean diameter of approximately 3.0 cm. In contrast, more than half of duodenal gastrinomas are smaller than 1.0 cm,⁵ with small size making the radiological diagnosis more difficult.⁶ The diagnosis of primary hepatic gastrinoma is especially problematic, because it is difficult to absolutely exclude the possibility of a primary gastrinoma in the pancreas, duodenum or other location, particularly because the liver is a frequent site of metastatic gastrinomas. Most reported hepatic gastrinomas were defined as primary when no tumors except for those in the liver had been detected preoperatively, intraoperatively, postoperatively or when postoperative serum gastrin levels declined to the normal range.¹ There has been only one published case preoperatively diagnosed with the primary hepatic gastrinoma. Shibata et al. defined their case as primary preoperatively, after ruling out gastrinomas in the gastrinoma triangle based on percutaneous transhepatic venous samplings.⁷

Selective arterial calcium injection tests, along with negative imaging modalities, are useful in diagnosing primary gastrinomas of the pancreas and duodenum.⁸ As we cannot obtain secretin in our country currently, we use calcium gluconate as a secretagogue. Gastrinomas have a calcium channel, therefore, high extracellular calcium concentrations cause degranulation of gastrinoma cells and subsequent release of gastrin. Calcium injection into vascular territories without gastrinomas has been reported to cause no rise in gastrin; thereby, we can find the vascular territories of

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the gastrinomas. SACI tests were regarded as not being useful for the diagnosis of primary hepatic gastrinomas. Because the calcium injected into arteries flows into the liver via the portal vein and stimulates secretion of gastrin, calcium injection into any artery was thought to increase serum gastrin concentration. We found, however, that the concentration of gastrin in the hepatic vein did not increase after calcium injection into any artery except for the proper hepatic arteries. These findings suggest that the amount of calcium that reached the hepatic tumor via the portal vein was too small to increase the concentration of gastrin in the hepatic vein. Actually, the vascular structure of hepatic neuroendocrine tumor such as gastrinoma is characterized by abundant tumor vessels that lack a portal blood supply and provide purely arterial nourishment.

More than half of duodenal gastrinomas are smaller than 1.0 cm, with small size making the radiological diagnosis more difficult. No paper discussed the relative merits of the sensitivity and specificity of SACI test and Ga-DOTATOC PET-CT. We considered that two inspections are necessary, both to complement the other, and so we should perform both to prove the primary hepatic gastrinoma. The SACI test helped exclude gastrinomas in the gastrinoma triangle, and Ga-DOTATOC PET-CT confirmed that there were no primary gastrinomas out of the gastrinoma triangle and no metastases.

In conclusion, primary hepatic gastrinomas are very rare and difficult to diagnose. We were able to preoperatively diagnose one of these lesions using the SACI test. This finding indicates that the SACI test is useful in the diagnosis of primary hepatic gastrinoma.

ACKNOWLEDGMENTS

We thank Yuji Namamoto, M.D., of the Department of Diagnostic Imaging and Nuclear Medicine Graduate School of Medicine, Kyoto University, Kyoto, Japan, for his considerable help.

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