LETTER TO THE EDITOR

Korean J Intern Med 2015;30:118-121
http://dx.doi.org/10.3904/kjim.2015.30.1.118

KJIM

An insulinoma with an aberrant feeder from the splenic artery detected by super-selective arterial calcium stimulation with venous sampling

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To the Editor,

A pancreatic insulinoma is a rare endocrine neoplasm with an estimated incidence of four cases per million person-years. Because the typical size of an insulinoma is < 2 cm, computed tomography (CT) or magnetic resonance imaging (MRI) may not detect the location of the tumor. The sensitivity of detecting an insulinoma is 70% to 80% for CT, 85% for MRI, and 85% to 90% for endoscopic ultrasound (EUS) [1]. Selective arterial calcium stimulation with hepatic venous sampling (ASVS) is a good complementary tool that increases the sensitivity to 84% to 100% [2]. However, ASVS does not always locate the insulinoma, and equivocal findings are reported frequently. We hereby report a case of an insulinoma in the pancreatic head with an aberrant feeder artery arising from the splenic artery, which was detected by angiography and super-selective ASVS.

A 50-year-old woman, who had never been diagnosed with diabetes mellitus, was admitted to a local emergency department for loss of consciousness. Her capillary blood glucose level was 41 mg/dL, and she recovered consciousness immediately after intravenous glucose administration. An abdominal CT scan did not indicate any definite pancreatic mass (Fig. 1A). Therefore, she was referred to our hospital for further evaluation.

Her medical history was unremarkable, and she had no family history of endocrine disease. She had suffered from fatigue and dizziness for the last 6 months. No specific findings were revealed on a physical examination. Laboratory results, including a complete blood cell count and basic chemistry

Received: February 11, 2014
Revised : June 2, 2014
Accepted: July 10, 2014

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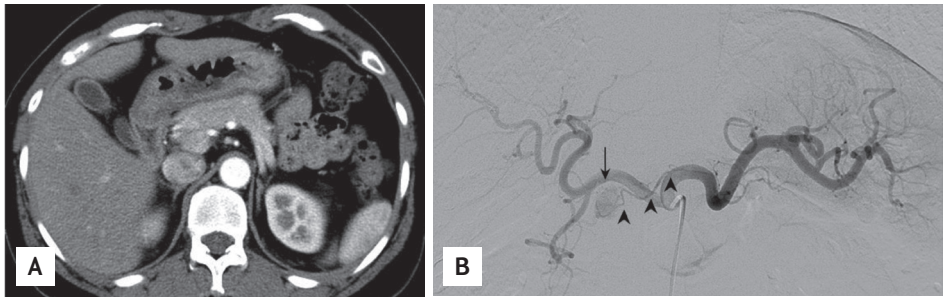

Figure 1. (A) Abdominal computed tomography image. (B) No definite mass was found. Celiac arteriography shows the tumor (arrow) and the feeding artery (arrowheads) originating from the proximal splenic artery.

pISSN 1226-3303
eISSN 2005-6648
http://www.kjim.org

tests, were within normal ranges.

A 72-hour fasting test was performed but was terminated after 2 hour due to symptomatic hypoglycemia. Her serum glucose level was 51 mg/dL, and she felt severe fatigue. Serum insulin (9.9 μIU/mL) and C-peptide (2.2 ng/mL) levels were elevated sufficiently to diagnose inappropriate endogenous hyperinsulinemia. Because we thought that the size of the potential insulinoma was very small, no further imaging studies, including EUS, were performed.

ASVS was performed to identify and localize the insulin-secreting tumor. First, celiac and superior mesenteric arteriography was performed. A small hypervascular tumor in the pancreatic head and a feeding artery originating from the proximal portion of the splenic artery were observed (Fig. 1B). Blood samples were obtained from the hepatic vein 0, 30, 60, and 120 seconds after injecting 5 mL calcium gluconate diluted in normal saline (0.025 mEq/kg) via the superior mesenteric artery, gastroduodenal artery, splenic artery, and the feeder artery originating from the splenic artery. Serum insulin and C-peptide levels are shown in Fig. 2.

Insulin and C-peptide levels in the splenic artery during conventional ASVS were higher than those in the superior mesenteric or gastroduodenal arteries. We took a step further using super-selective ASVS on the aberrant feeder artery from the splenic artery. The results showed remarkable increases in insulin and C-peptide secretion (Fig. 2), indicating that the tumor stained in the pancreatic head was an insulinoma.

A pylorus-preserving pancreaticoduodenectomy was performed without complications. The pathology was consistent with a well-differentiated benign endocrine tumor based on the 2000 World Health Organization Classification for Pancreatic Endocrine Neoplasms. The tumor was 1.4 × 0.7 × 0.5 cm^3 in size, the mitotic count was < 1/10 at a high power field, and Ki-67 was positive in 0.27% (15/5,524) of the tumor cells. Immunohistochemical studies revealed that most of the tumor cells were positive for chromogranin, synaptophysin, insulin, and CD56, but negative for glucagon, somatostatin, carcinoembryonic antigen, and mucin-1 (Fig. 3). The premeal capillary blood glucose level recovered after surgery and was maintained within 100 to 150 mg/dL. Her fasting plasma glucose level was 89 mg/dL at the 3-month follow-up. Serum insulin and C-peptide levels decreased to 1.4 μIU/mL and 1.2 ng/mL, respectively. She did not experience hypoglycemic symptoms.

This was a case of a pancreatic head insulinoma supplied by an aberrant artery from the splenic artery. Conventional ASVS assumes two distinctive portions of the pancreas: the pancreatic head portion supplied by the superior mesenteric or gastroduodenal artery and the pancreatic body to tail portion supplied by the splenic

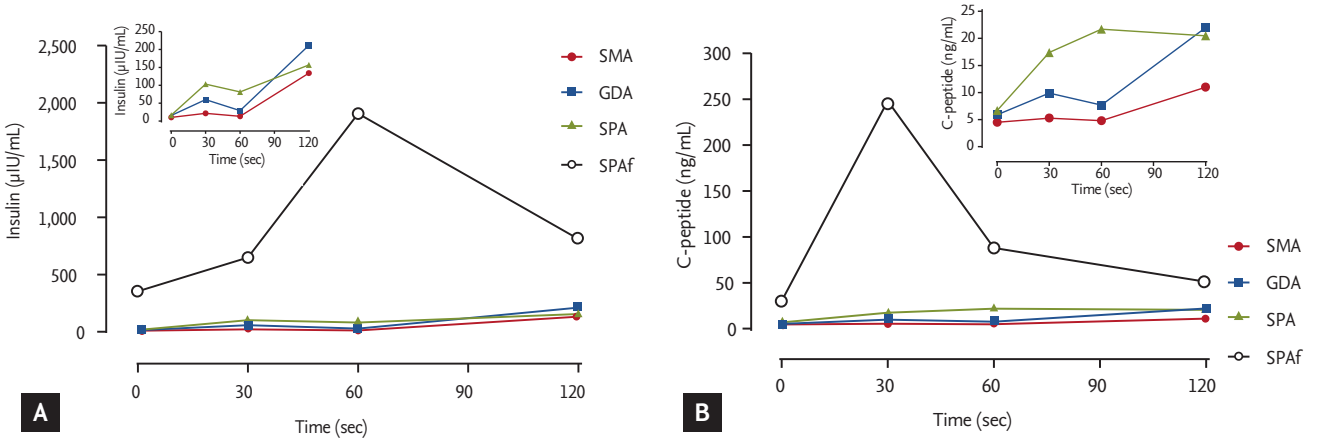

Figure 2. Insulin (A) and C-peptide (B) levels in hepatic venous blood samples after selective arterial calcium stimulation of three major pancreatic arteries and the feeder artery. Insets depict insulin and C-peptide levels after calcium stimulation of three major pancreatic arteries. SMA, superior mesenteric artery; GDA, gastroduodenal artery; SPA, splenic artery; SPAf, the feeder artery from the splenic artery.

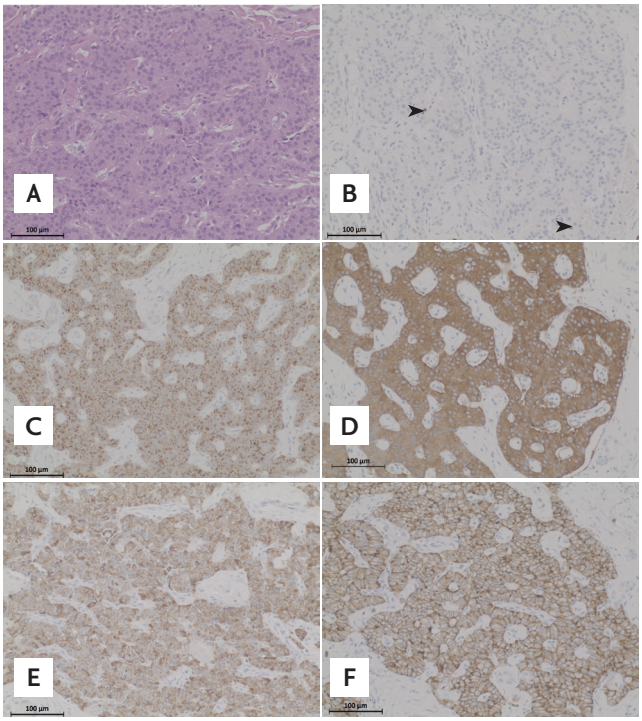

Figure 3. (A-F) Immunohistochemical staining of the insulinoma (×200). Hematoxylin and eosin staining of the insulinoma is consistent with a neuroendocrine tumor (A). The proportion of Ki-67-positive cells (arrowheads) was 0.27% (15/5,524) of tumor cells (B). Most of the tumor cells stained positively for chromogranin (C), synaptophysin (D), insulin (E), and CD56 (F).

artery. However, many variations in pancreatic vascular anatomy have been reported, particularly in the head portion. Okahara et al. [3] found that 36% of inferior pancreaticoduodenal arteries arose from branches other than the superior mesenteric artery, and that 2% of the superior pancreaticoduodenal arteries arose from branches other than the gastroduodenal artery. An insulinoma with an aberrant feeder artery, as in our case, has not yet been reported.

Two studies on super-selective ASVS have been published [4,5]. However, these studies performed intra-arterial calcium stimulation through the splenic artery divided into proximal, middle, and distal portions, whereas we selected the tumor feeding artery specifically. Notably, the results of conventional ASVS indicated that the insulinoma could be in the pancreatic body or the tail portion, because higher insulin and C-peptide levels were obtained via the splenic artery compared with the superior mesenteric or gastroduodenal arteries. However, peak insulin levels 60 seconds after the calcium injection via the feeder artery was in hundreds of basal insulin levels of the three major arteries supplying the pancreas. We could have resected the pancreatic body and tail if we had not found tumor staining in the pancreatic head and its feeder artery. As such, super-selective ASVS was necessary to localize and functionally diagnose the insulinoma accurately.

Interestingly, baseline insulin and C-peptide levels were highly elevated compared with those of the three major arteries supplying the pancreas during super-selective ASVS for the feeder artery. One study reported elevated insulin levels in tumor-supplying arteries before calcium stimulation, as in our case [4]. This finding can be explained by delayed calcium perfusion into the insulinoma from prior stimulation tests or by the radiocontrast media used during angiography. A 15-minute interval between stimulations has been suggested to avoid this delayed effect [4].

In conclusion, this case report emphasizes the importance of careful angiography and super-selective ASVS to diagnose suspicious insulinomas that are difficult to locate using conventional imaging methods.

Keywords: Insulinoma; Angiography

Conflict of interest

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Cryer PE, Axelrod L, Grossman AB, et al. Evaluation and management of adult hypoglycemic disorders: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2009;94:709-728.
2. Brandle M, Pfammatter T, Spinas GA, Lehmann R, Schmid C. Assessment of selective arterial calcium stimulation and hepatic venous sampling to localize insulin-secreting tumours. Clin Endocrinol (Oxf) 2001;55:357-362.
3. Okahara M, Mori H, Kiyosue H, Yamada Y, Sagara Y, Matsumoto S. Arterial supply to the pancreas; variations and

http://dx.doi.org/10.3904/kjim.2015.30.1.118

cross-sectional anatomy. Abdom Imaging 2010;35:134-142.
4. Defreyne L, Konig K, Lerch MM, et al. Modified intra-arterial calcium stimulation with venous sampling test for preoperative localization of insulinomas. Abdom Imaging 1998;23:322-331.
5. Morita S, Machida H, Kuwatsuru R, et al. Preoperative localization of pancreatic insulinoma by super selective arterial stimulation with venous sampling. Abdom Imaging 2007;32:126-128.