Usefulness of the Combination of Pre- and Intraoperative Selective Intraarterial Calcium Injection to Detect Residual Insulinomas

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Abstract

In a 35-year-old woman diagnosed with insulinoma selective intraarterial calcium injection was positive for proximal gastroduodenal artery and inferior pancreaticoduodenal artery involvement preoperatively. Although non-invasive imaging studies were negative, a mass was detected at the pancreatic uncus by intraoperative ultrasonography. Gastroduodenal artery calcium injection was performed after enucleation of the tumor. Following calcium injection, the insulin level was inappropriately increased and further pancreaticoduodenectomy was performed. After excision, another tumor was detected at the head of the pancreas by histopathological examination. As shown, selective intraarterial calcium injection is useful to localize tumors preoperatively and intraoperatively.

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Case Report

A 35-year-old Japanese female had episodes of loss of awareness over 10 months. She had had a traffic accident while driving alone and was brought to our hospital on May 13, 1997. Family and past histories were not remarkable. The patient weighed 57.0 kg and her body height was 158 cm (body mass index: 22.8 kg/m²). The level of consciousness was E1V2M5 (by Glasgow Coma Scale). Results of routine laboratory tests including blood chemistry, hemogram, and serology were normal except for a plasma glucose of 27 mg/dl (70-110 mg/dl) and an immunoreactive insulin (IRI) of 8.7 μU/ml (0-17 μU/ml). Anti-insulin antibody and anti-insulin receptor antibody tests were negative. Continuous intravenous injection of 10% glucose was given to maintain a plasma glucose level of over 70 mg/dl in order to prevent hypoglycemia and associated symptoms. Then, a fasting glucose tolerance test was performed. Based upon the collected data, the biochemical criteria for the diagnosis of insulinoma were met. Namely, the patient had symptomatic hypoglycemia (plasma glucose 47 mg/dl) with inappropriately elevated IRI (11 μU/ml) (0-17 μU/ml) and C-peptide (2.2 ng/ml) (0.6-2.8 ng/ml) after 6 hours. Serum levels of HCG and HCG-β were normal. Function of the pituitary, adrenal, thyroid, and parathyroid glands were normal. Ultrasonography (US), endoscopic ultrasonography (EUS), computed tomography (CT), magnetic resonance imaging, digital subtraction angiography, and CT angiography failed to localize the tumors. There was no evidence of hepatic metastasis on CT scan or by angiography. The percutaneous transhepatic venous sampling (PTVS) was also negative. Finally, selective intraarterial calcium injection was performed. We used the method described by O’shea et al (1). A catheter was placed in the right hepatic vein close to its junction with the inferior vena cava via a femoral vein. Each artery [proximal gastroduodenal artery (GDA), inferior pancreatico-duodenal artery (IPDA), proximal splenic artery, left hepatic artery, superior mesenteric artery] was catheterized in turn. After samples were taken twice from the hepatic vein as control values, calcium gluconate was injected into the artery, as a bolus at time zero. The dose of calcium used was 1.0 mg/kg for the first three studies. This was reduced to 0.25 mg/kg for subsequent studies. Blood samples were taken from the right hepatic vein before calcium injections and at 30, 60, 90, and 120 seconds after each injection. A 9-fold increase in insulin release was noted with injection of the IPDA, and a 3-fold insulin increase was detected upon GDA injection as shown in Fig. 1. Thus, the patient was expected to have a tumor at the head of the pancreas or at the uncus.

An open intra-abdominal operation was performed on July 29, 1997. A low echoic mass (12x12 mm) was detected at the uncus by intraoperative ultrasonography (IOUS) (Fig. 2). No other tumors were detected. At first, enucleation of the tumor was undertaken. However, after enucleation, the serum IRI level did not decrease to half of the preenucleation value (Fig. 3). Next, gastroduodenal arterial calcium injection and portal venous sampling were performed. The insulin release was increased by 6.5-fold at this time (Fig. 4). The existence of other tumors was suspected and the pancreaticoduodenectomy was

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Figure 1. Insulin release after preoperative intraarterial calcium injection. Insulin release determined after preoperative intraarterial calcium injection. 60-second samples from the right hepatic vein showed 9-fold (IPDA) and 3-fold (GDA) increases in insulin levels. IRI: immunoreactive insulin, GDA: Gastroduodenal artery, IPDA: Inferior pancreaticoduodenal artery, LHA: Left hepatic artery, SA: Splenic artery, SMA: Superior mesenteric artery.

Figure 2. Intraoperative ultrasonography. Hypoechogenic lesion of the pancreatic uncus, 12 mm in diameter.

The enucleated sample was confirmed to be an islet cell adenoma, as immunostaining examination was positive for insulin, but negative for glucagon and somatostatin. Another adenoma (0.7x0.7 mm) was detected at the head of the pancreas by histopathological examination (Fig. 5). There were no operative complications. She has had no more symptoms of hypoglycemia thus far and the rapid intravenous calcium infusion test which was done after 1 year was negative (Fig. 6) (2).

Discussion

Insulinoma is a rare disease, but still the most frequent cause of pancreatic endocrine tumors. Surgical resection of the tumor is likely to be curative, but these tumors are generally benign and small. It is difficult to localize the tumors preoperatively, especially small ones (<2 cm) (3). About 10% of patients with insulinomas have tumors that can not be localized (4). Successful detection rates of insulinoma reported in the literature range from 16–80% for CT, 30–60% for US, 77–89% for EUS, 29–91% for angiography and 64–100% for PTVS.
with Zollinger-Ellison syndrome. In turn, intravenous calcium is known to effectively stimulate the release of insulin from insulinomas (20). According to the methodology of intraarterial secretin injection, it was first reported by Doppman et al to select calcium gluconate as the intraarterial insulin secretagogue (16). The method is highly sensitive for the detection of tumor, and is also useful to detect hepatic metastasis.

The tumors in the present case were only sensitive to selective intraarterial calcium injection preoperatively. Only the first tumor could be detected by IOUS. However, the levels of the serum IRI did not decrease sufficiently after enucleation and, thus, gastroduodenal arterial calcium injection was performed. This injection was positive even after enucleation of the tumor, suggesting that there were other functional tumors in the head or uncus in addition to the enucleated one. Based upon this information, the pancreaticoduodenectomy was extended, and another islet cell adenoma was detected by histopathological examination. After the operation, the patient has had no hypoglycemic attacks, and a rapid intravenous calcium infusion test was negative. The size of the tumor (0.7 x0.7 mm) is the smallest reported except for autopsy materials (21), but levels of serum IRI after enucleation and the response to gastroduodenal artery calcium injection pointed to the presence of residual functional tumor. On the other hand, we have to consider the possibility that the small tumor is of little clinical significance.

This case is reported to provide information about the use of selective intraarterial calcium injection intraoperatively as well as preoperatively to detect residual tumors. The implementation of both pre- and intraoperative calcium stimulation tests should allow surgeons to be more confident about performing curative surgical procedures.

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References


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