Overtly Manifested Diabetes Mellitus after Resection of Insulinoma

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Abstract

Insulinoma is the most common cause of endogenous hyperinsulinemic hypoglycemia in adults. However, the coincidence of insulinoma and diabetes is extremely uncommon. We describe a rare, but very interesting case of diabetes mellitus which was masked by insulinoma and was overtly manifest after the removal of the insulinoma.

Key words: insulinoma, hypoglycemia, diabetes mellitus

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Introduction

Insulinoma is the most common cause of endogenous hyperinsulinemic hypoglycemia in adults. While its incidence is estimated at four per one million person-years (1), the coincidence of insulinoma and diabetes is an extremely rare event limited to only a few reports (2-7). Here, we report case of a patient who was diagnosed with diabetes mellitus within nine days after wedge resection of insulinoma.

Case Report

A 74-year-old woman was admitted to the emergency department at an outside hospital because of decreased mental status. Admission labs revealed hypoglycemia with a plasma glucose level of 40 mg/dL. Her past medical history included hypertension for four years which was well-controlled with amlodipine 5 mg PO QD. Family and social histories were unremarkable. Her body weight and body mass index (BMI) were 73.6 kg and 32.7 kg/m², respectively. The remainder of the physical examination was normal. The patient’s mental status quickly recovered to baseline after intravenous injection of 50% dextrose solution, and the plasma glucose level increased to 152 mg/dL.

During the hypoglycemic episode, the serum insulin concentration measured 22.7 μU/mL (determined by radioimmunoassay using human insulin specific RIA kit from Linco Research, St. Charles, MO, USA; cross-reactivity with proinsulin, <0.02%; lower limit of sensitivity, 14.4 pmol/L; intra-assay coefficient of variation, 4.5%; interassay coefficient of variation, <10%; normal range, 1-2 μU/mL), and the C-peptide level was 6.0 ng/mL (determined by radioimmunoassay using human C-peptide specific RIA kit from Linco Research; very low cross-reactivity<4.0% to human proinsulin; normal range, 1-2 ng/mL). HbA1c was 4.1% on admission. Other laboratory findings were unremarkable. Abdominal computed tomography (CT) showed a 2 cm sized pancreatic head mass (Fig. 1A). There was no evidence suggestive of multiple endocrine neoplasia-type 1.

The patient was referred to our hospital for surgical removal of the pancreatic mass. Abdominal magnetic resonance imaging (MRI) showed a 2 cm sized hypervascular single mass in the pancreatic head (Fig. 1B). Laparoscopy revealed a whitish-yellow colored mass located on the inferior border of the posterior wall of the pancreas. It was found to be adherent to the surrounding pancreatic tissue. Due to suspicion of active bleeding from the feeding artery during the operation, the laparoscopic procedure was converted to open surgery, and the 1.6×1.8×1.4 cm mass was
about 2 cm sized, well-defined, solid, hypervascular mass in the pancreatic head. (A) Abdominal CT. (B) Abdominal MRI.

Figure 2. Immunohistochemical staining of resected tumor. (A) Positive immunostaining for anti-insulin antibody (×400 magnification). (B) Positive immunostaining for synaptophysin (×400 magnification).

removed. Pathologic diagnosis was consistent with insulinoma (Fig. 2).

On the fourth postoperative day, intravenously injected 10% dextrose solution was stopped. On the ninth postoperative day, fasting plasma glucose, insulin, and C-peptide levels were 157 mg/dL, 19.83 μU/mL, and 3.01 ng/mL, respectively. Levels of plasma glucose, insulin, and C-peptide of postprandial 2 hours were 253 mg/dL, 33.96 μU/mL, and 3.21 ng/mL, respectively. She had no symptoms of pancreatic exocrine insufficiency, however, hyperglycemia persisted even after recovery from surgery. At that time, her body weight and BMI were 70.0 kg and 31.1 kg/m², respectively. The patient subsequently developed overt diabetes. There was neither microalbuminuria nor diabetic retinopathy on fundus examination. She is currently being managed with metformin 500 mg PO BID and sitagliptin 100 mg PO QD without any further hypoglycemic events. The current HbA1c is 6.0%.

Discussion

Hypoglycemia is a common clinical entity, most frequently due to a complication of treatment for diabetes (8, 9). Insulinoma is the most common cause of organic hyperinsulinemic hypoglycemia. Its diagnosis depends on the exclusion of other causes of hypoglycemia, such as the surreptitious administration of insulin or oral anti-diabetic agents, and the presence of inappropriately elevated plasma insulin and C-peptide levels with hypoglycemia (8). Noninvasive studies including transabdominal ultrasound, CT, and MRI often fail to localize insulinoma, because its size is usually less than 1 cm (10). Endoscopic ultrasound (EUS) is considered the best diagnostic modality for tumor localization with a detection rate of 70-90% (11, 12).

Currently, laparoscopic enucleation, when feasible, is the technique of choice in the treatment of insulinoma (10, 13). Complications of pancreatic resection include pancreatic leak, intraabdominal fluid collection, pleural effusion, pancreatic pseudocyst, bleeding, and diabetes (14). Diabetes can develop after pancreatic surgery depending on the extent of resection (15).

We encountered a very interesting case manifested with diabetes mellitus after wedge resection of insulinoma in a patient with no prior history of hyperglycemia or diabetes despite regular, routine medical care. Her high BMI (32.7 kg/m²), increased insulin resistance and increased plasma glucose levels after mass removal indicate that she may have had diabetes before surgery. We infer that the diabetes may
have been masked by the insulinoma before surgery and then manifested as overt diabetes after its resection. It is unlikely that the patient’s hyperglycemia after surgical treatment of the insulinoma was simply a complication of pancreatic resection, as based on the following reasons: 1) since only a wedge resection of the tumor was performed, the majority of the pancreas was left intact, and 2) postoperative plasma insulin and C-peptide levels were well within a range which would maintain normal glucose levels in the absence of well-established insulin resistance. There have been a few case descriptions of patients with insulinoma and preexisting diabetes (2-7). This, however, is the first case report to our knowledge of a patient with an insulinoma that had completely masked type 2 diabetes mellitus which was rendered overt after removal of the insulinoma. Although this is an extremely rare case, clinicians may suspect underlying diabetes mellitus in a patient presenting with insulinoma if there are other risk factors for insulin resistance or diabetes present, and appropriate perioperative risk management strategies can be employed.

References