

A case of insulinoma confused with dumping syndrome after total gastrectomy

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Abstract

We present the case of a 70-year-old female patient with persistent hypoglycemia after total gastrectomy due to gastrointestinal stromal tumors. She was thought to have late dumping syndrome but was diagnosed with insulinoma after further examination. Dumping syndrome is mainly seen after stomach or esophageal surgery. It is divided into early dumping and late dumping syndrome. Late dumping syndrome is initially manifested by an exaggerated insulin response and reactive hypoglycemia after glucagon-like peptide-1 release. Diagnosis is based on clinical findings. Treatment mainly consists of reducing carbohydrate intake and not ingesting solid and liquid foods together. In cases where diet alone is not sufficient, acarbose, an α -glucosidase inhibitor that slows the digestion of carbohydrates, may be beneficial for late dumping. Octreotide can be used in resistant cases. However, the diagnosis of insulinoma, which leads to a similar clinical presentation in resistant dumping cases, should be kept in mind. Our patient who showed clinical signs of dumping syndrome after gastrectomy, and treatment-resistant hypoglycemia was diagnosed with insulinoma on the basis of further investigations. The patient's symptoms resolved after surgery for insulinoma.

Keywords: Dumping syndrome, Gastrectomy, Hypoglycemia, Insulinoma

Introduction

Gastrointestinal stromal tumors (GISTs) are the most widely occurring mesenchymal tumors affecting the gastrointestinal tract. They are generally frequently observed in the stomach and proximal small intestine. However, albeit rarely, they can be seen anywhere in the gastrointestinal tract [1]. Gastrointestinal bleeding is a common clinical finding. However, small asymptomatic lesions are frequently detected incidentally. Treatment is planned using a multidisciplinary approach. Surgery is the only curative treatment particularly for resectable masses [2].

Dumping syndrome is a common complication in patients following gastric surgery. It is seen in approximately 25%–50% of patients after surgery, and 5%–10% of these patients exhibit marked clinical symptoms. The severity of dumping syndrome varies depending on the type of surgery. The syndrome occurs in 75% of patients in the early period following gastric bypass surgery. The condition persists for approximately 12–18 months, while recovery occurs subsequently in most patients [3].

Insulinoma is a rare neuroendocrine tumor characterized by hyperinsulinism-related hypoglycemic episodes. It is generally detected as a benign solitary tumor and can also be seen together with multiple endocrine neoplasias (MEN) [4].

We describe the case of a patient who had undergone total gastrectomy due to GIST approximately 1 year previously and who was followed-up with a diagnosis of dumping syndrome throughout the previous 2 months. Insulinoma was detected using advanced tests that were performed due to continuous worsening of the patient's symptoms. This case will contribute to the existing literature as a case of insulinoma presenting as dumping syndrome following gastrectomy due to GIST.

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Informed Consent

The authors stated that the written consent was obtained from the patient presented with images in the study.

Conflict of Interest

No conflict of interest was declared by the authors.

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Case presentation

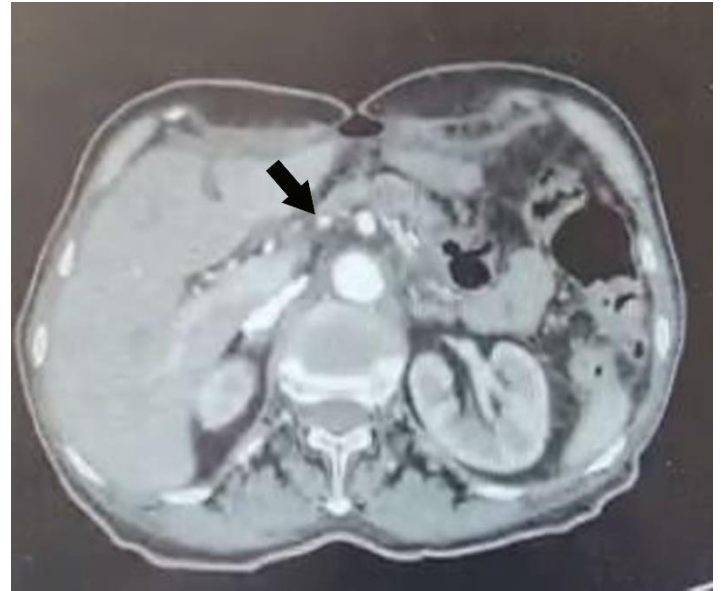
A 70-year-old woman presented with occasional malaise, palpitations, and sweating over the previous 2 months. The patient had presented twice to the emergency department with her current symptoms, and we were consulted when low blood sugar was determined.

The patient had undergone a right mastectomy due to breast cancer 13 years previously and total gastrectomy due to GIST 1 year earlier. The patient was receiving regular imatinib therapy. The patient had a history of total gastrectomy, and her symptoms were initially thought to be possibly associated with dumping syndrome. Hypoglycemia symptoms together with low blood sugar were observed at least twice a day, approximately 2 h after eating. The patient's blood sugar during hypoglycemia was 45 mg/dL, insulin was 2.6 mIU/L, and c-peptide was 1.4 μ U/mL. Adrenal reserve evaluation was requested to investigate a potential tyrosine kinase side effect in this patient using imatinib. Adrenal failure was excluded when the patient's cortisol levels at the time of hypoglycemia were 34 mg/dL. Late dumping syndrome was then suspected. The interval between the patient's meals was reduced to 4 h, and pre-meal acarbose therapy was initiated. However, low blood sugar values persisted at follow-up. The prolonged fasting test was performed. Blood sugar at hour 5 was 40 mg/dL, insulin was 3.7 μ U/mL, and c-peptide 1.7 ng/mL. Magnetic resonance imaging of the pancreas was performed with a preliminary diagnosis of insulinoma. Galyum-68 DOTA TATE PET/B (DOTAPET) was also performed, and these results revealed a 12-mm lesion in the pancreas. The case was evaluated as insulinoma on the basis of these results (Figure 1, 2). The patient was referred to the general surgery clinic, and the mass was removed with enucleation. The patient's pathology report indicated a "well-differentiated neuroendocrine tumor, insulinoma".

Figure 1: MR imaging revealed pancreatic insulinoma



Figure 2: PET imaging revealed pancreatic insulinoma



Discussion

The present case is important in terms of insulinoma being diagnosed in a patient presenting with dumping syndrome-like symptoms following gastric surgery and in terms of diagnosing a neuroendocrine tumor in a patient previously diagnosed with GIST and breast cancer. This is the only case to date of insulinoma that was diagnosed in a patient who underwent surgery for GIST and breast cancer.

There are two types of dumping syndrome. Early dumping syndrome emerges 15 min after food intake. This results from the rapid emptying of foods into the small intestine. Symptoms of colic-type abdominal pain, nausea, tachycardia, and diarrhea are generally present. Precautionary measures such as reducing the amount of carbohydrate in meals and increasing the patient's fiber intake, shortening the interval between meals, and fluid intake 30 min after solid food intake are generally sufficient. Patients generally tend to recover 3 months after surgery [5].

Late dumping syndrome is rare after gastric surgery. It is seen in 0.1%–0.3% of patients, and generally in Roux-en Y gastric bypass patients. Symptoms emerge approximately 1–3 hours after carbohydrate-rich meals in particular, and the basic cause is hyperinsulinemic hypoglycemia. The etiology is not fully understood. Similar to early dumping syndrome, dietary changes are recommended. Medical treatment can also be considered in non-responsive patients (such as nifedipine, acarbose, and diazoxide). If medical treatment is unsuccessful, invasive procedures such as feeding by inserting a tube into the residual stomach and re-operation can also be applied [5, 6].

Insulinoma is a rare neuroendocrine tumor, and the etiology of solitary adenomas is not fully understood. It can be seen as a component of MEN type 1 (MEN1) syndrome. Hypoglycemia develops with high insulin concentrations. Insulin is normally released from pancreatic cells with high blood glucose. For insulinoma, however, insulin production continues although blood glucose is low. When intracellular insulin storage pools are full, insulin is released into the blood. Hyperinsulinemia increases glycogen synthesis while reducing gluconeogenesis and glycogenolysis [7].

The reported annual incidence of insulinoma is 1–4 per million. Insulinoma generally appears as a solitary benign tumor, although 5.8% of cases have been shown to be malignant. Other benign tumors may be co-present in 7% of cases, and a relationship with MEN1 syndrome has been shown in 6%–7.6% of cases. Patients are diagnosed on average between 40 and 50 years of age [8].

GIST represents approximately 20% of soft tissue sarcomas. The annual incidence is approximately 10 per million. Micro-GISTs less than 1 cm in size and with low mitotic activity and mild clinical symptoms are more common in middle or more advanced age. Micro-GISTs constitute 10%–35% of all GISTs. They are most frequently located in the stomach and proximal small intestine, although they can be present anywhere in the gastrointestinal tract. Fewer than 5% are present outside the gastrointestinal tract, and these are known as extra-GISTs [9].

Hypoglycemia can occur following gastric bypass surgery, although cases of severe hypoglycemia are rare. The pathophysiology remains unclear. Patients must be closely followed-up, and insulinoma, although rare, must be ruled out. Dietary adjustment is important in patients with suspected dumping syndrome in particular. However, as in our patient, diet modification may not always be effective, especially in individuals experiencing severe neuroglycopenic symptoms. Interventional procedures should also be considered, particularly in patients developing pancreatic islet cell hypertrophy [10].

Endogenous hyperinsulinemic hypoglycemia may rarely be seen, particularly following Roux-en-Y gastric bypass surgery. If this condition is observed, the most common cause is islet cell hyperplasia (nesidioblastosis). A rare cause of endogenous hyperinsulinemic hypoglycemia is an insulinoma. Thirty-six patients undergoing pancreatic surgery due to nesidioblastosis over approximately 13 years were evaluated in one study. A previous history of gastric bypass surgery was present in 27 patients [11].

GISTs can occur together with several malignancies. Comorbidity with neuroendocrine tumors may be determined in the presence of neurofibromatosis. However, co-existent neuroendocrine tumor and GIST in the absence of neurofibromatosis is rare, with only one case having been reported. Insulinoma was diagnosed in a patient who was followed-up due to hypoglycemia, and concomitant GIST was detected [12].

GIST and insulinoma without neurofibromatosis were present in our patient. However, because the patient had undergone surgery due to GIST approximately 1 year previously, she was followed-up with a diagnosis of dumping syndrome for 2 months. Insulinoma was diagnosed after tests were performed due to worsening of the patient's symptoms. The present case is important as the first in which a neuroendocrine tumor was detected in a patient diagnosed with GIST who had undergone gastric bypass surgery with a dumping syndrome-like presentation.

Conclusion

Despite its rarity, patients should be examined for possible insulinoma, especially in the presence of severe hypoglycemia and dumping syndrome after gastric bypass surgery.

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