

# Roux-en-Y gastric bypass as a cure of iatrogenic steroid-induced diabetes

## Authors' Contribution:

A – Study Design  
B – Data Collection  
C – Statistical Analysis  
D – Data Interpretation  
E – Manuscript Preparation  
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## ABSTRACT:

**Background:** Steroid-induced diabetes (SIDM) is a frequently found clinical condition since steroid-based therapies continue to be widely used in hospital and ambulatory care. Recommended optimal treatment of SIDM includes similar glucose lowering strategies as in type 2 diabetes. This typical management cannot cure the disease, it can only control blood glucose. Recently, bariatric surgery has emerged as an effective treatment for type 2 diabetes mellitus. However, up to now, the usefulness of bariatric surgery in treatment of SIDM has not been evaluated.

**Case report:** A 49-year-old female oncologic patient with steroid induced diabetes was referred for surgical treatment to the Department of General and Transplant Surgery in November 2009. Six years earlier, she underwent successful oncologic treatment with cladribine and high doses of steroids due to hairy cell leukemia. Finally complete hematologic remission with normalization of morphology and reduction of spleen size has been obtained. Prior to steroid treatment, blood glucose and urine examinations were within normal range. The patient was non-obese and had no family history of diabetes. Nevertheless, the patient developed diabetes secondary to corticosteroid therapy, poorly controlled by oral hypoglycemic agent (acarbose), successfully converted to insulin therapy. Upon admission to the Department of General and Transplant Surgery, the patient was treated with 58 units of insulin per day. The patient was scheduled for Roux-en-Y gastric bypass (RYGB). Insulin was withdrawn immediately after the surgery and within six months after the surgery, plasma glucose and glycated hemoglobin (HbA<sub>1c</sub>-5.5%) levels reached and remained within normal range. Currently, eight years after surgery, body weight and BMI are 80 kg and 27.68 kg/m<sup>2</sup>, respectively. Plasma glucose and glycated hemoglobin are also normal. Importantly, from an oncological point of view, the patient has remained in continuous complete remission since October 2003.

**Conclusions:** Our report is the first to our knowledge describing the effect of gastric bypass surgery on SIDM in a patient with prior hematologic malignancy. It proves that surgically altered anatomy of the small intestine improves glucose homeostasis previously disturbed with pro-diabetic medication.

## KEYWORDS:

bariatric surgery, cure, iatrogenic diabetes, Roux-en-Y gastric bypass, steroid induced diabetes, treatment

## INTRODUCTION

Drug-induced diabetes is a frequently found clinical condition since multiple medications induce hyperglycemia through a variety of mechanisms [1, 2]. Steroid-induced diabetes mellitus (SIDM) has been well recognized more than 60 years ago. Steroid-based therapies continue to be widely used in hospital and ambulatory care also including combination chemotherapy in the management of oncological and hematological patients.

The recommended optimal treatment of SIDM in oncologic patients includes similar glucose lowering strategies as in type 2 diabetes. And similarly, like in any other type of diabetes, this typical management cannot cure the disease, it can only control blood glucose. Bariatric surgery has recently emerged as an effective treatment for primary type 2 diabetes mellitus, we also reported one of the first case series of successful bariatric surgery use in obese type 1 diabetes patients [3]. Roux-en-Y gastric bypass is superior to intensive medical therapy alone in achieving glycemic control [4]. However, up to now, the usefulness of bariatric surgery in treatment of SIDM including oncologic patients has not been evaluated, along with expanding therapeutic indications for steroids use. Hereby, we present a case report of a patient with steroid-induced diabetes mellitus, which developed after combination chemother-

apy of hematologic malignancy and was successfully cured with Roux-en-Y gastric bypass.

## CASE REPORT

A 49-year-old female oncologic patient with steroid-induced diabetes was referred for surgical treatment to the Department of General and Transplant Surgery in November 2009. Six years earlier, she underwent successful oncologic treatment including high doses of steroids used for several months due to fever of unknown reason. The first time she was admitted to the Department of Hematology was in January 2003, with unexplained recurrent fever up to 40°C. The patient presented with pancytopenia, splenomegaly (163x71 mm), and recurrent reaction to prednisone (with a returning = fever, when the steroid dose was lowered below 40 mg/day). Differential diagnosis included tuberculosis (with 8 weeks of failed tests with pirazinamid), hypoplastic myelodysplastic syndrome or hairy cell leukemia. Finally, in September 2003, upon bone marrow examination, diagnosis of hairy cell leukemia has been established based on the presence of 36% of cells with typical hairy morphology and immunophenotype. This was followed by administration of five doses of cladribine (2-CdA), once a week, in a dose of 0.12 mg/kg of body mass. Finally, complete hematologic remis-

sion with normalization of morphology and reduction of spleen size has been obtained. Prior to steroid treatment, blood glucose and urine examinations were within normal range. The patient was non-obese and had no family history of diabetes. Nevertheless, the patient developed diabetes secondary to corticosteroids therapy, poorly controlled via an oral hypoglycemic agent (acarbose), successfully converted to insulin therapy.

Upon admission to the Department of General and Transplant Surgery, the patient was treated with 58 units of insulin per day. Other comorbidities included arterial hypertension (treated with long-acting ACE-inhibitor, diuretic and nonselective beta blocker), diabetic neuropathy (glycated hemoglobin was 8.3%), combined hyperlipidemia (cholesterol – 207 mg/dL, LDL – 117 mg/dL, HDL – 38 mg/dL, triglycerides – 261 mg/dL; treated with low fat diet), hepatosteatosis (confirmed by abdominal ultrasonography) and osteoarthritis (confirmed by X-ray imaging studies). The patient was scheduled for Roux-en-Y gastric bypass (RYGB). This surgery consists in division of the stomach with a stapler and creation of a small gastric pouch (volume of 30 ml) anastomosed directly with a loop of jejunum. Such an alteration in the anatomy of the upper part of the digestive tract results in bypassing the stomach and duodenum. RYGB leads to marked reduction in stomach volume (restrictive effect) accompanied by altered hormonal function of the gastrointestinal tract, manifested mostly with elevated incretin hormone levels. Total operative time was 55 minutes, the recovery period was uneventful and patient was discharged on the 6th post-operative day. Insulin was withdrawn immediately after the operation and within six months after the surgery, plasma glucose and glycated hemoglobin (HbA1c-6.1%) levels reached and remained within normal range. Currently, eight years after surgery, body weight and BMI are 80 kg and 27.68 kg/m<sup>2</sup>, respectively. Fasting plasma glucose (90 mg/dL), glycated hemoglobin (HbA1c-5.1%), plasma cholesterol (185 mg/dL) and triglycerides (145 mg/dL) levels are also normal. Importantly, from an oncological point of view, the patient has remained in continuous complete remission since October 2003.

## DISCUSSION AND CONCLUSIONS

Glucocorticoids have many adverse effects including Cushing's syndrome, hypertension, depressed mood or weight gain. The frequency of diabetes among patients treated with glucocorticoids varies from 1.5% to 47%. These discrepancies may be a result of

the heterogeneity of assessed populations, primary diseases, management, and the accepted definition of diabetes. Classical risk factors for SIDM include the duration of steroidotherapy, the absolute dose, and the relative potency of the glucocorticoid. However, recent studies indicate that in many patients SIDM appears not to be directly dose-related and most of these risk factors are not readily identified [5].

Gastric bypass has been repeatedly shown to greatly improve diabetes control and may actually cure the disease among obese patients. There are many hypotheses that may explain this phenomenon. "Foregut hypothesis" is based on the fact, that exclusion of the duodenum and proximal jejunum down-regulates the GIP synthesis, which favors insulin resistance. "Hindgut hypothesis" claims that chyme in the distal intestine increases the secretion of GLP-1, which stimulates insulin secretion and has a positive impact on the proliferation of pancreatic beta cells. According to Wen et al., down-regulation of renal gluconeogenic enzymes together with amelioration of insulin signal pathway in the renal cortex and an elevated level of circulating adiponectin might explain the antidiabetic effect of gastric bypass. Patients who underwent bariatric surgery had significantly better results at three years in comparison to the group treated with pharmacotherapy only [4]. According to the national guidelines for diabetes management, gastric bypass should be taken into consideration if the patient has type 2 diabetes and a BMI exceeding 35 kg/m<sup>2</sup> (1). More recently, improvement of glucose control in diabetic patients after this bariatric surgery has been demonstrated also in non-obese patients with gastric cancer.

Treatment of SIDM is a challenging clinical problem, with no specified treatment guidelines. The recommended option is insulin therapy from the time of diagnosis, combined with a maintenance therapy with glucocorticoids. However, according to Ito et al., doses of steroids should be divided and given in combination therapy with acarbose and/or nateglinide. These medications are efficient in controlling postprandial hyperglycemia, although their efficacy is inadequate when the patient develops SIDM early after initiation or intensification of steroid therapy.

Our report is the first to our knowledge describing the effect of gastric bypass surgery on SIDM in a patient with prior hematologic malignancy. It proves that surgically altered anatomy of the small intestine improves glucose homeostasis previously disturbed with pro-diabetic medication.

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