Case report

Metabolic surgery provides remission of pancreatogenic diabetes in a nonobese patient

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In recent years, metabolic surgery has been found to effectively provide remission of type 2 diabetes mellitus (T2DM) in obese individuals and has proven superior to intense medical therapy [1,2]. However, the results of metabolic surgery on other types of diabetes beyond T2DM are scarce, and although multiple reports have found moderate to no improvement in insulin requirements, none have found insulin independence after metabolic surgery beyond T2DM [3]. As metabolic surgeons, we have learned a great deal about the mechanisms of resolution of T2DM in obese patients. It seems reasonable and at the same time controversial to generalize some of these principles to other types of diabetes such as pancreatogenic diabetes.

Case presentation and management

The Ethics Committee approved this procedure. The patient was an 18-year-old nonobese woman who as a neonate presented with severe hypoglycemic episodes as a result of pathologically confirmed nesidioblastosis. Shortly after, she underwent subtotal pancreatectomy. At 7 years of age, she became insulin dependent. A preoperative abdominal computed tomography scan found a radiologically normal remnant head of the pancreas without pathology or enlargement.

Esophagogastroduodenoscopy and portal vein Doppler studies did not reveal any abnormalities. Preoperative abdominal computed tomography scan found a radiologically normal remnant head of the pancreas without pathology or enlargement.

Postoperatively the patient resumed insulin and oral metformin (500 mg) twice daily. Insulin was rapidly weaned until discontinued on postoperative day 42. Metformin was also tapered until discontinued at 7 months. Hemoglobin A1c decreased from baseline levels of 8.4% to 5.4%, whereas C-peptide increased from .4 to 1.1 ng/mL. Postoperative pre- and postprandial glucose and insulin levels were 111 and 112 mg/dL and 2.9 and 7.7 μU/mL, respectively. Lipid profile also improved compared with preoperative values (cholesterol 228 versus 155 mg/dL; high-density lipoprotein 39 versus 49 mg/dL; low-density lipoprotein 156 versus 80 mg/dL, and triglycerides 160 versus 134 mg/dL, respectively). Total weight loss was 22 kg (from 67 to 45 kg) and her body mass index decreased from 29 to 20 kg/m2. The patient was insulin independent and off metformin at the 8-month follow-up.

Discussion

Nesidioblastosis is a hyperinsulinemic hypoglycemic state of infancy that is unresponsive to medical management,
necessitating a subtotal pancreatectomy. Interestingly, nesidioblastosis has also been reported after RYGB surgery for obesity [4]. It is possible that β-cell trophic factors such as glucagon-like peptide 1 may be brought into play, leading to the growth of pancreatic β-cells and consequent hyperfunction of islets, ultimately culminating in postprandial hypoglycemia.

On the other hand, after a pancreatectomy, the loss of pancreatic parenchyma causes a disruption of glucose homeostasis known as pancreatogenic diabetes [5]. This form of glucose intolerance is different from the other forms of diabetes mellitus, in that affected individuals suffer frequent episodes of hypoglycemia. The development or worsening of diabetes after pancreatectomy is extremely common, with different types of resections conveying different risks for disease progression [6]. For instance, distal pancreatectomy places patients at a greater risk for the development of new-onset postoperative diabetes compared with pancreatectoduodenectomy. Conversely, patients with preoperative diabetes are more likely to experience worsening of their disease after pancreatectoduodenectomy compared with distal pancreatectomy.

Several hypotheses support the use of the RYGB procedure, in which a duodenoejunal exclusion is performed [7]. We elected to provide a complete duodenoejunal exclusion by creating an elongated 150-cm bilipancreatic limb, which may provide the greatest metabolic and incretin effect. We have previously described the importance of this elongated bilipancreatic limb during revisional procedures to improve both weight loss and diabetes remission [8]. Of note, our bilipancreatic limb is lengthened 3- to 5-fold compared with the standard RYGB reconstruction used to treat severe obesity, which typically measures between 30 and 50 cm in length. The 300-cm common channel’s length is not related to any malabsorption issues.

Various types of intestinal reconstructions in metabolic surgery have proven effective in the treatment of nonobese and mildly obese patients with T2DM. The duodenoejunal exclusion that explains in part the T2DM remission after Roux-en-Y gastric bypass metabolic surgery may be then extrapolated to other types of diabetes such as the one presented here. We believe the key component of this metabolic surgery is the extended length of the bilipancreatic limb and not that of the alimentary limb.

Although these pancreatectomized patients with long-standing diabetes do have minimal pancreatic tissue mass and therefore insulin secretion, it is feasible that they may still have a significant β-cell population in the pancreatic remnant that is not fully differentiated. It appears that the incretin/anti-incretin and β-cell trophic effects of this type of metabolic surgery provide a proper endocrine environment to facilitate full differentiation of these remnant cells and restore some insulin secretion, which leads to independence [9]. This effect may explain in part the existence of an enteropancreatic axis as described by Rubin et al [10].

There may be other hormonal, paracrine, or immune pathways involved that have not been yet explained and need to be examined. It is also plausible that β-cell trophic factors (likely glucagon-like peptide 1) at the pancreatic remnant as well as decreased caloric intake and weight loss are in part responsible for the observed metabolic response. The most fascinating finding of the present case is the trophic effect of this specific type of intestinal bypass over dormant or undifferentiated pancreatic islets and over peripheral insulin sensitivity.

In summary, insulin independence and diabetes remission was achieved in a patient after subtotal pancreatectomy after RYGB. To our knowledge, this is the first case in the literature in which short-term diabetes remission has been achieved with metabolic surgery in a nonobese patient after pancreatectomy. We hypothesize that the lengthened bilipancreatic limb Roux-en-Y reconstruction as part of a multimodal approach may provide improvements for the other insulin-dependent conditions such as type 1 diabetes mellitus. Such studies are currently ongoing at our institute. The long-term metabolic outcomes of this type of surgery for this particular case scenario are unknown and should be investigated further.

References