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Case Report: Nesidioblastosis in Adult Patient

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ABSTRACT

Nesidioblastosis is a rare disease among adults, affecting between 0.5 and 5.0% of the age group, causing persistent organic hyperinsulinemic hypoglycemia. The frequent clinical presentation is postprandial hypoglycemia, and the preoperative diagnosis is challenging and through exclusion criteria, since there is no clinical context or highly specific exams. We present a clinical case of a male patient, 47 years old, diagnosed with Nesidioblastosis, in 2014, after frequent loss of consciousness and without association with fasting. The patient was submitted to Frey's technique, after failure with other procedures. The method adopted proved to be effective for correcting the patient's endocrine problem, as well as without sequelae to the gastrointestinal tract.

Keywords

Nesidioblastosis, Insulin, Hypoglycemia.

Introduction

Hypoglycemia in non-diabetic patients is not a common clinical problem and can be a diagnostic and therapeutic challenge [1]. Persistent organic hyperinsulinemic hypoglycemia (PHH) is a disorder of the endocrine pancreas that occurs in newborns and adults. In newborns, PHH is most caused by malfunctioning β-cells, a condition that is known by the expressions congenital hyperinsulinism (CH) [2,3] or nesidioblastosis [4,5]. Among adults, PHH can be caused by an insulinoma or, rarely, by nesidioblastosis [6-8].

Adult patients with nesidioblastosis, which is characterized by endogenous hyperinsulinemic hypoglycemia that is not caused by an insulinoma, have β-cell hypertrophy, islets with enlarged and hyperchromic nuclei, and growing islets that sprout from the periductal epithelium [10-12]. The predominant clinical feature of this disease is postprandial hypoglycemia and biochemical findings like those of insulinoma. According to published statistics, 0.5 to 5.0% of nesidioblastosis cases occur in adults [13]. Because of this, a case of nesidioblastosis is reported in an adult male with a two-year history of intermittent episodes of symptomatic hypoglycemia, requiring several surgical interventions for an effective treatment.

Case Presentation

Male patient, 47 years old, with a mean body mass index (BMI) of 41.4 kg/m², started his clinical context in 2012, reporting episodes of loss of consciousness, about six to eight times a day, with a blood glucose test. capillary, often less than 30 mg/dL, randomly and unrelated to fasting. The symptoms worsened, leading him to search medical help, being investigated and the hypothesis of nesidioblastosis was raised.

In 2014, he was referred to Hospital Sírio Libanês (São Paulo-SP, Brazil), where he underwent tests, which found nesidioblastosis affecting the tail and head of the pancreas. Therefore, he started to receive clinical-pharmacological treatment with Diazoxide and

Octreotide. However, the patient's symptoms worsened, leading him, in 2015, to a body-caudal pancreatectomy and Roux-en-Y gastric bypass. After the procedure, he reports that he remained asymptomatic for three months, when hypoglycemic symptoms reappeared.

In 2016, the patient presented with semi-intestinal occlusion, requiring two surgical interventions - in one of them, the Roux-en-Y gastric bypass was undone due to intestinal invagination. In 2017, he evolved with severe hypoglycemia, returning to search specialized medical care. He denied associated comorbidities. In view of the situation, a selective calcium stimulation test was performed [Figure 1] which showed excess insulin production in the region irrigated by the superior mesenteric artery (SMA) and gastroduodenal artery (GDA).

In addition, a computed tomography of the abdomen was performed [Figure 2], which did not show neoplasic processes, with only changes in the abdominal anatomy due to previous surgeries being observed - in addition to the surgeries already mentioned in 2015 and 2016, there was also a partial left nephrectomy for removal of a sarcoma in 1999.

After that, an open surgical reintervention was chosen in orde to reduce the volume of pancreatic tissue still existing through a subtotal pancreatectomy with duodenal preservation. The procedure undertaken with the patient in the supine position and under general anesthesia. A Chevron laparotomy was performed, with resection of the anterior scar, then the retractors were placed and the dissection was initiated with the release of previous adhesions. In the following time, a wide Kocher and Catell maneuver was performed and, afterwards, the dissection of the superior mesenteric vessels was initiated, also proceeding with the ligation of the vessels that communicated with the pancreas. The dissection was performed with UltraCision® throughout the procedure, and the resection of the head and the uncinate process of the pancreas was performed according to the Frey technique [Figure 3].

During the procedure, the patient's blood glucose was measured every thirty minutes and after resection of the uncinate process, as well as a sub-total portion of the head of the pancreas, blood glucose increased to levels above 200mg/dL. Then, biological glue was placed on the resected area and cholecystectomy and cholangiography [Figure 4] were performed to verify the integrity of the retro-pancreatic bile duct. In addition, an appendectomy was performed and, due to the complexity of the case, it was decided to place a 24 Fr Blake® drain close to the resection and exiting through the counter-opening, connecting to the reservoir. Finally, the abdominal wall was closed.

In the pathological examination of the seven sections of the pancreas (uncinate process and head) removed during surgery, hyperplasia of pancreatic islets and nuclear hypertrophy of beta cells were observed. In immunohistochemistry, the results were positive for the following antibodies: cytokeratins AE1/AE3, chromogranin A, synaptophysin, CD56 and insulin, being negative for: glucagon and Ki-67. These findings, together with the clinical data, support the diagnosis of Nesidioblastosis. After the surgical procedure, the patient presented eradication of hypoglycemic episodes, with a controlled diet and using insulin, Dapaglifozin and Pancreatin.

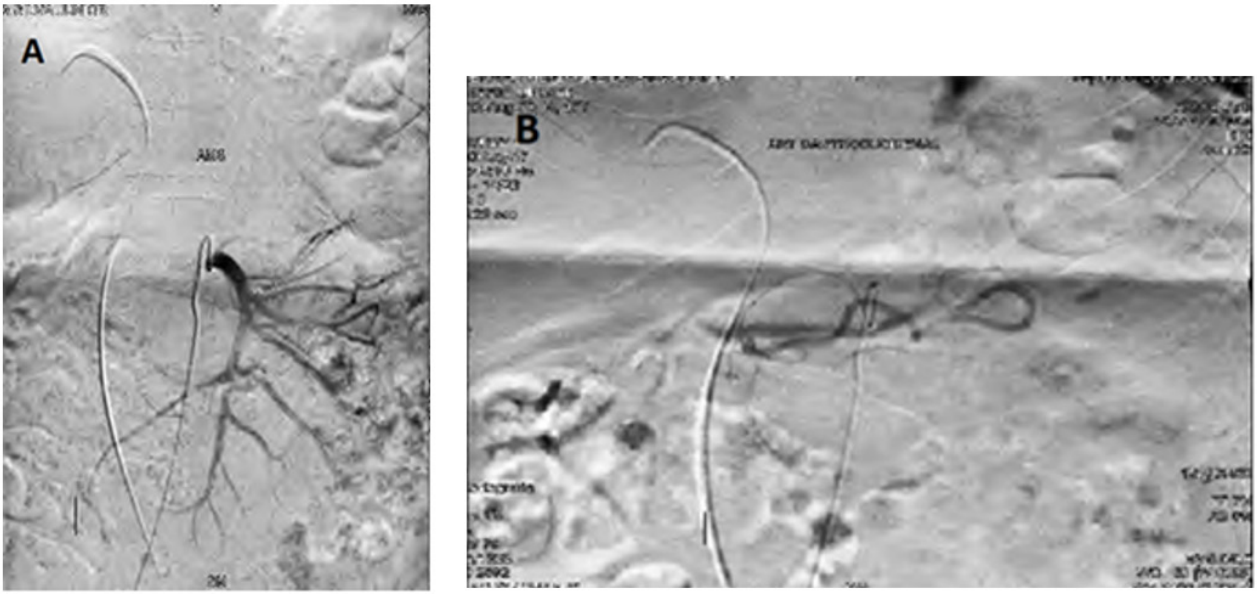

Figure 1: Selective calcium stimulation test, basal insulin test and 30 and 60 seconds after calcium infusion were performed. In the AMS (A) the values were, respectively, 9.95, 11.78 and 50.02. In the AGD (B) they were, respectively, 2.47, 11.74 and 2.41.

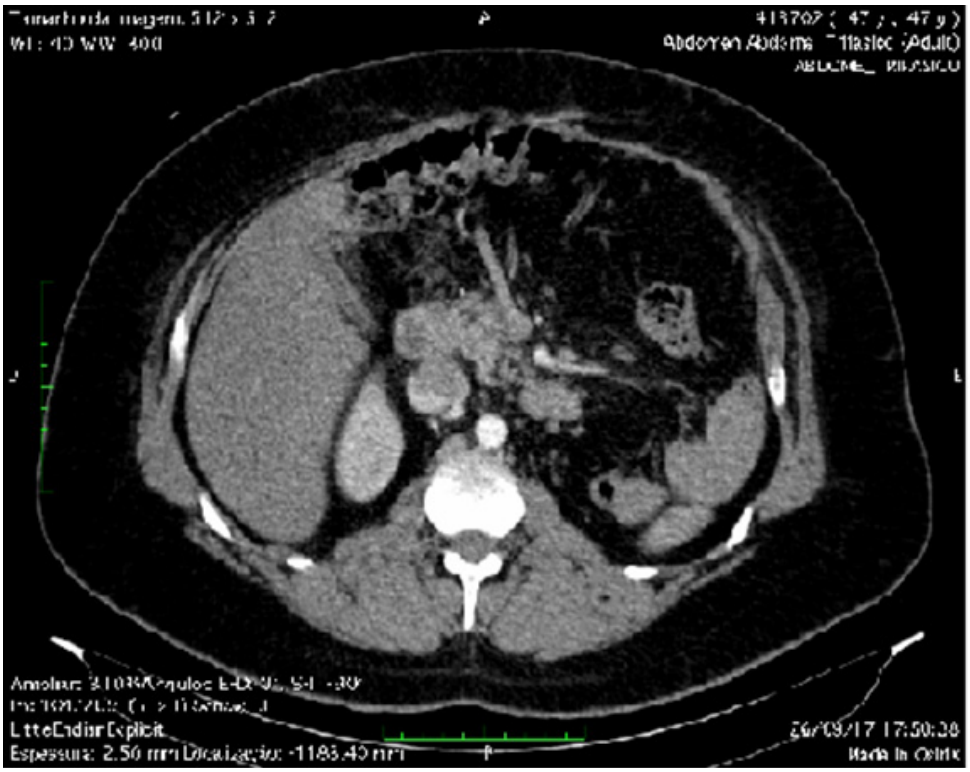

Figure 2: Abdominal CT showing head and uncinate process with pancreas with preserved density, with usual contrast enhancement. Pancreatic body and tail not visible. Post-nephrectomy status.

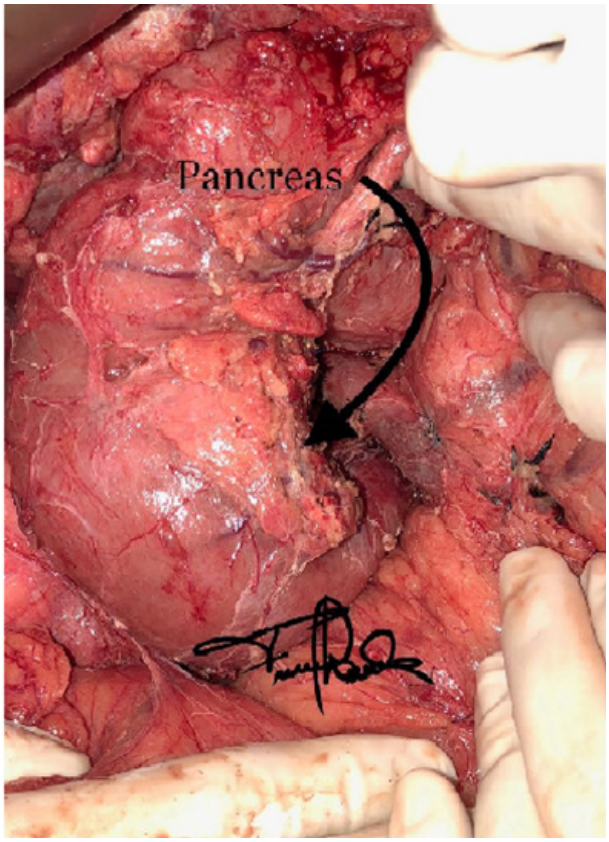

Figure 3: Image after surgical procedure using the Frey Technique.

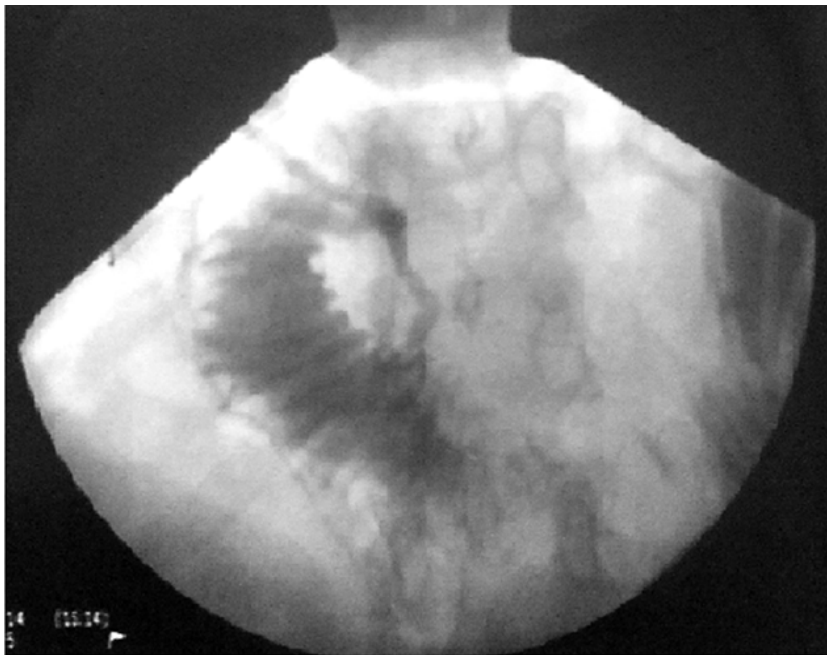

Figure 4: Cholangiography showing the integrity of the intrapancreatic portion of the common bile duct.

Discussion and Conclusion

According to published statistics, 0.5 to 5.0% of nesidioblastosis cases occur in adults [13], and it is therefore a rare disease among adults that causes HPH. The first description of a case related to nesidioblastosis occurred in 1938 in children [14], only in 1975 was the first case described in adults [15]. In this age group, nesidioblastosis is characterized by a functional disorder of beta cells that can occur as a feature of noninsulinoma pancreatogenous hypoglycemia syndrome (NIPHS) or after Roux-en-Y gastric bypass surgery, both of which cause endogenous hypoglycemia. However, the most common cause of this condition in adults is local or multiple insulinoma [16].

The predominant clinical feature is postprandial hypoglycemia. In a series of 18 Mayo Clinic patients, aged 16 to 78 years, BMI of 25.7 kg/m², with a male predominance (70%), symptoms occurred postprandially, two to four hours after meals, and rarely fasting [10,11]. In contrast, most patients with insulinoma have fasting hypoglycemia. In the case reported, the patient did not present specific moments of hypoglycemic symptoms, which occurred randomly.

The preoperative diagnosis of adult nesidioblastosis is challenging, as there are no determining clinical symptoms or history and there are no highly specific functional tests [18]. The patient reported in the case presented unspecific complaints and functional tests were not performed previously, as the patient already had a previous diagnosis of nesidioblastosis. A selective arterial calcium stimulation test can indicate hyperactive β-cell activity and provide guidance for disease localization and direct resection of appropriate pancreatic regions [19]. Such examination determined an increase in insulin production in the regions irrigated by AMS and GDA, which correspond to irrigation of the head and uncinate process.

The diagnostic criteria for adult nesidioblastosis proposed by Klöppel et al. [17] involve exclusion of an insulinoma and several histological features. Thus, the definitive diagnosis of adult nesidioblastosis is better defined postoperatively after performing a histological examination. All the criteria proposed by Kloppel et al. [17] were evidenced in the pathological study of the removed piece, in addition, immunohistochemistry also contributed to the diagnosis of nesidioblastosis, since diffuse neuroendocrine tissue was observed.

For the treatment of nesidioblastosis in patients with mild to moderate symptoms, nutritional modification is a reasonable initial intervention. Nutritional modification, particularly reducing free carbohydrate intake and spacing carbohydrate intake evenly throughout the day. If mild to moderate symptoms persist, we prescribe Acarbose, an alpha-glucosidase inhibitor. Other medications such as: octreotides, Verapamil, Diazoxide and Acarbose improved symptoms of hypoglycemia in patients with hypoglycemia after Roux-en-Y bypass. However, the definitive treatment for severe and moderate cases refractory to other therapies is the surgical procedure. As the patient in this report was not successful with the clinical treatment initially proposed, surgical intervention was chosen. Although there is no standard surgical technique, partial or subtotal pancreatectomy was able to resolve most cases [10,11] however, some require multiple surgical interventions due to symptoms of recurrent hypoglycemia after surgery. Due to these multiple interventions, the extent of pancreatic resection requires caution to preserve sufficient β-cell volume to prevent diabetes. The case of the reported patient behaved similarly, since he needed two approaches, the last one being a subtotal pancreatectomy with duodenal preservation, based on the Frey technique, proposed by Frey et al. [20] for the treatment of chronic pancreatitis. Such intervention proved to be

effective and reduced the patient's symptoms and also helped in glycemic control, since the patient had a small part of the pancreas still preserved. Thus, it is evident that the surgical technique used (Frey's technique) was efficient for the patient's glycemic control and without sequelae to the gastrointestinal tract, however, despite the preservation of pancreatic tissue, the reported case developed diabetes after pancreatic tissue resections.

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