Case Report

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Nesidioblastosis post-bariatric surgery in an adult patient: a case report and review of literature

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Introduction and importance: Adult-onset nesidioblastosis is an exceedingly rare yet significant cause of persistent hyperinsulinemic hypoglycemia. This condition is often associated to bariatric surgeries such as Roux-en-Y gastric bypass and sleeve gastrectomy. Characterized by abnormal β-cell hyperplasia and hypertrophy, its diagnosis presents a unique challenge due to overlapping features with insulinomas and post-bariatric hypoglycemia syndrome (PBHS).

Case presentation: We report a 55-year-old woman with a history of gastric sleeve and Roux-en-Y gastric bypass surgeries who presented with a 1.5-year history of recurrent hypoglycemic episodes. Her symptoms, including blurred vision, tremors, and altered consciousness, persisted despite medical therapy with octreotide, acarbose, and nifedipine. Extensive imaging, including magnetic resonance imaging and endoscopic ultrasound, ruled out insulinomas, raising suspicion of non-insulinoma pancreatogenous hypoglycemia syndrome. The patient underwent laparoscopic subtotal distal pancreatectomy with spleen preservation. Histopathological examination confirmed nesidioblastosis, revealing irregular islet distribution and β-cell hypertrophy. Post-surgery, the patient achieved normoglycemia without recurrence of hypoglycemic episodes during follow-up.

Discussion: This case highlights the complexity of diagnosing nesidioblastosis in adults, especially following bariatric surgeries. Nesidioblastosis involves β-cell hyperplasia and hypertrophy driven by hormonal factors like GLP-1, whereas PBHS results from altered incretin patterns causing excessive insulin release. Advanced imaging and multidisciplinary collaboration are important for accurate diagnosis. Surgical management remains a cornerstone for refractory cases, as demonstrated in this patient's remarkable recovery.

Conclusion: Nesidioblastosis is a rare condition but should be considered in the differential diagnosis of post-bariatric surgery hypoglycemia. This case highlights the importance of distinguishing nesidioblastosis from PBHS to ensure appropriate and effective management strategies.

Keywords: bariatric surgery, case report, nesidioblastosis, non-insulinoma pancreatogenous hypoglycemia, persistence hypoglycemia

Introduction

Adult-onset nesidioblastosis is an uncommon complication that can arise following bariatric surgeries, especially Roux-en-Y gastric bypass surgery (RYGB), which typically occurs after months to years after the procedure[1,2]. This condition is characterized by hyperinsulinemic hypoglycemia, where excessive insulin secretion leads to persistently low blood sugar levels. Patients with nesedioblastosis mostly present with postprandial hypoglycemia and other symptoms such as blurry vision, altered consciousness, fatigue, and seizure[2-4]. This condition is very rare, with an estimated annual incidence of less than 0.1 cases per 1 000 000 individuals, and it most often manifests around the age of 47[1,5]. Nesidioblastosis involves the dysfunction of pancreatic β-cells, where these cells undergo abnormal growth and enlargement throughout the pancreas without evidence of tumor formation. This leads to an increase in islet cells and associated nuclear changes, such as enlargement and hyperchromasia of β-cells[6-8]. While nesidioblastosis is a well-known cause of persistent hyperinsulinemic hypoglycemia (PHH) in newborns, it is rarely encountered in adults. In such cases, it is

HIGHLIGHTS

- Adult-onset nesidioblastosis is a rare and significant cause of persistent hyperinsulinemic hypoglycemia.
- Differentiating between nesidioblastosis, post-bariatric hypoglycemia, and dumping syndrome is important as they share overlapping symptoms but differ in pathophysiology and management.
- Early recognition, comprehensive diagnostics, and a multidisciplinary approach are essential for effective management of nesidioblastosis.

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often confused with insulinoma, which is the more prevalent cause of PHH in the adult population (Table 1).

Here, we report the case of a patient presenting with prolonged symptoms of hypoglycemia. The patient had a history of bariatric surgery, specifically a gastric sleeve followed by a RYGB. Through imaging studies and histopathological evaluation, a multidisciplinary team diagnosed post-bariatric surgery nesidioblastosis, which was effectively managed with laparoscopic subtotal pancreatectomy.

This work has been reported in line with the SCARE criteria[9].

Case presentation

A 55-year-old patient presented with a 1.5-year history of recurrent hypoglycemic episodes that had recently worsened, resulting in symptoms such as blurred vision, tremors, and occasional loss of consciousness. The patient's medical history included previous bariatric surgeries: a gastric sleeve followed by a gastric bypass for weight loss. She denied taking any hypoglycemic medications. Despite treatment with octapeptide, acarbose, and nifedipine prescribed by her endocrinologist, symptom relief was minimal, and the hypoglycemic episodes persisted. Extensive diagnostic evaluations were conducted to identify the cause of the hypoglycemia. Laboratory tests, magnetic resonance imaging (MRI), and endoscopic ultrasound were performed. These investigations ruled out insulin-secreting tumors or other masses commonly associated with hypoglycemia, providing no evidence of a neoplastic source. This has led to suspicion of a diagnosis of non-insulinoma pancreatogenous hypoglycemia syndrome (NIPHS).

Due to failure of pharmacological treatments and the severity of the symptoms, the patient was counselled about surgical options. After thorough discussion, the decision was made to proceed with a subtotal distal pancreatectomy with spleen preservation, a procedure that has shown promise for managing NIPHS. During surgery, the distal pancreatic tissue appeared grossly normal as seen in (Fig. 1C). A Laparoscopic approach for subtotal resection of the pancreas was performed, with meticulous preservation of the spleen and blood supply as seen in (Fig. 1)

Macroscopic examination of distal pancreatectomy specimen showed no masses or any parenchymal growth. Microscopic examination showed benign pancreatic tissue with increased numbers of pancreatic islet cells distributed irregularly throughout the pancreas; some of them were enlarged with irregular shape (Fig. 2).

Based on the macroscopic and morphological features, combined with clinical and radiological findings, the final diagnosis was nesidioblastosis. This clinical term describes islet cells hypertrophy in the context of hyperinsulinemic hypoglycemia. Nesidioblastosis is commonly observed in infants born to diabetic mothers and is often associated with various syndromes. Similar morphological changes have also been reported in adult patients with persistent hyperinsulinemic hypoglycemia, as well as in adults who have undergone bariatric surgery.

The patient underwent a partial pancreatectomy and remained hospitalized for six days for close monitoring. Postoperatively, vital signs and random blood sugar levels were regularly assessed. Blood glucose levels remained relatively stable throughout the admission period, ranging between 101 mg/dL and 162 mg/dL. No severe hyperglycemia or hypoglycemia episodes were noted. The patient tolerated oral intake well, had no significant gastrointestinal complaints, and pain was managed adequately with analgesics. No postoperative infections, pancreatic fistula, or other complications were observed. The surgical site remained clean and dry. The patient was hemodynamically stable throughout hospitalization and was discharged on postoperative day six in good general condition. Follow-up evaluations at one and two months post-operation demonstrated significant clinical improvement, with no recurrence of hypoglycemic episodes.

Table 1

The differences between adult-onset nesidioblastosis and insulinoma

	Nesidioblastosis	Insulinoma
Hypoglycemia	Postprandial hyperinsulinemic hypoglycemia	Fasting hyperinsulinemic hypoglycemia
Age	Neonate	Adults
Nature of disease	Benign	Usually benign
Main location	Entire pancreas	Distributed to head, body, and tail of the pancreas
Leading cause	Mostly genetic (neonate) Bariatric surgery (adult)	Sporadic or genetic (MEN1)
Insulin, C-peptide	High	High
72 hour fasting	Mostly negative	Mostly positive
Gene mutation	SUR1, GCK, Kir6, GLUD1, MEN1 (rare)	MEN1
Gross findings	NA	Solitary encapsulated mass (usually <2 cm in size)
Histopathological findings	• Diffuse with different prevalence • Ductoinsular complex • Hypertrophied B-cell with giant nuclei	• Solid or gyriform pattern • Amyloid deposition in B-cell
Treatment	Medical management, partial or subtotal pancreatectomy	Partial pancreatectomy

Discussion

Obesity is a major health concern worldwide that leads to various conditions and elevates mortality rates, resulting in a higher demand for bariatric surgery which is considered an effective intervention for morbid obesity and its related health conditions. In the United States, bariatric surgery is one of the most common elective procedures[10], with approximately 350 000 bariatric surgeries performed annually, predominantly sleeve gastrectomy and RYGB[11]. Postoperative complications occur in approximately 10–20% of patients, with serious complications occurring in less than 2% of cases[12].

Nesidioblastosis is a rare complication that results in a persistent hyperinsulinemic, hypoglycemic following RYGB surgery and it is estimated to occur in 0.1–0.3% of post-RYGB patients[5,13]. The majority of nesidioblastosis cases occur following RYGB, but there is only one reported case that occurred after sleeve gastrectomy[10]. However, our case described a patient who underwent both sleeve gastrectomy followed by RYGB, so this condition can be a complication of both bariatric surgery types, sleeve gastrectomy and RYGB, which is a very rare clinical condition.

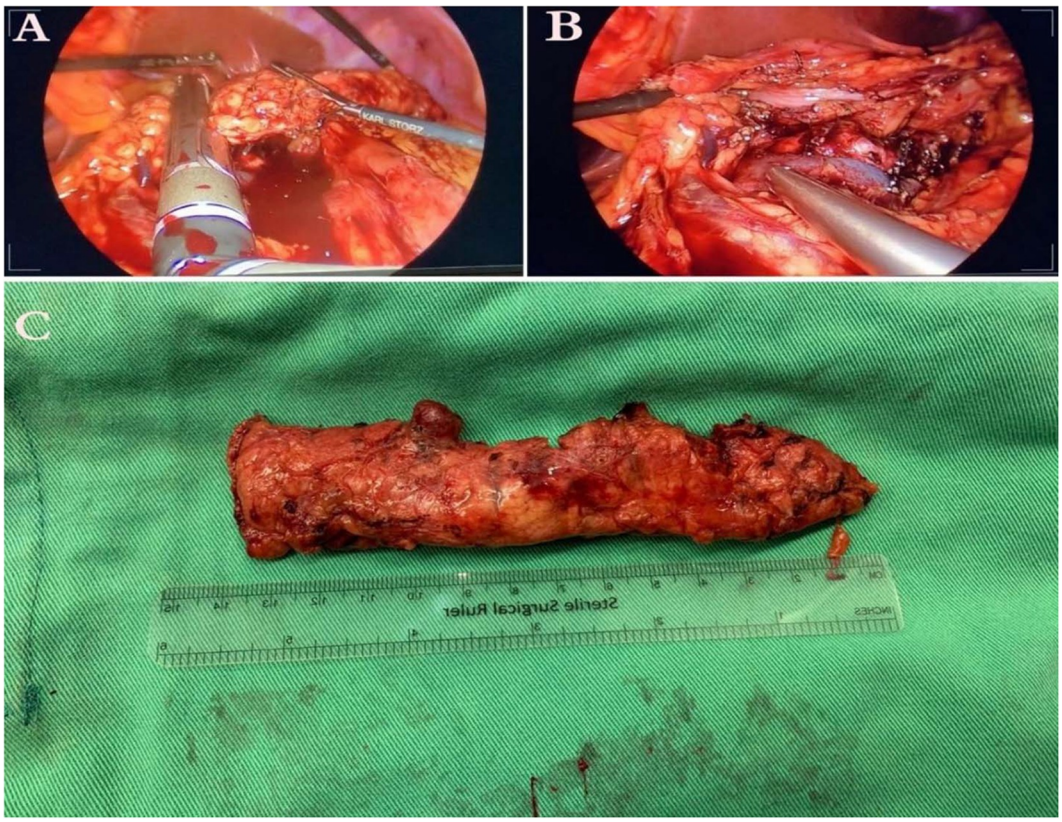

Figure 1. (A) Laparoscopic view of the pancreas and pancreatic tail before resection. (B) Laparoscopic view post-resection of the distal pancreas with preservation of splenic vascular supply. (C) Gross view of resected pancreatic segment measuring 13.5 cm in length.

The pathogenesis of nesidioblastosis remains incompletely understood. However, it is believed to be associated with elevated levels of glucagon-like peptide-1 (GLP-1), gastric inhibitory polypeptide (GIP), and ghrelin-stimulated increases in insulin release, which collectively stimulate increased insulin secretion. These events result in diffuse hyperplasia of the β-cells within the islets of Langerhans[3-5]. Additionally, histopathological research has indicated that individuals with nesidioblastosis following gastric bypass surgery show elevated levels of growth factors and their receptors, including insulin-like growth factor 2 (IGF2) and transforming growth factor-beta receptor 3, within pancreatic islets. This indicates that these growth factors might contribute to the onset of nesidioblastosis by stimulating beta-cell hyperplasia and hypertrophy[14]. In contrast, postbariatric hypoglycemia syndrome arises from excessive insulin release triggered by nutrient intake, associated with changes in incretin patterns, particularly an increase in GLP-1[13].

Patients with nesidioblastosis typically present with postprandial hyperinsulinemic hypoglycemia. Depending on the severity, mild to moderate hypoglycemia can result in symptoms similar to our case such as palpitations, anxiety, disorientation, starvation, sweating, excitement, tremors, and paresthesia. These symptoms are similar to those seen in dumping syndrome, a condition marked by quick gastric emptying that can lead to early post-meal symptoms like nausea, abdominal discomfort, diarrhea, flushing, palpitations, and tachycardia, along with later symptoms such as hypoglycemia, dizziness, and fatigue[15]. In contrast, in cases of severe hypoglycemia due to nesidioblastosis, symptoms include drowsiness, delirium, significant disorientation, seizures, and even coma[2,3,16].

Dumping syndrome can be diagnosed either through a clinical evaluation or by conducting gastric emptying studies and glucose tolerance tests[15]. Post-bariatric hypoglycemia necessitates ongoing glucose monitoring, insulin assays, and mixed-meal tolerance testing[13]. Alternatively, diagnosing nesidioblastosis can be challenging due to the limitations of traditional imaging techniques, which often lack the sensitivity required to distinguish between focal and diffuse hyperinsulinism[17]. A comprehensive diagnostic approach is necessary, including detailed history and physical examination which are essential to exclude other potential causes of hypoglycemia. Common imaging modalities including computerized tomography, MRI, and endoscopic ultrasound are used to rule out insulinomas. However, these are often negative in cases of nesidioblastosis[15,18], this aligns with our case that exhibited a normal appearance of the pancreas and biliary system on endoscopic ultrasound, and normal MRI imaging. Another potential test for nesidioblastosis is a selective arterial calcium stimulation test to detect the presence of hyperfunctioning islet cells[19]. A histopathological examination of the resected pancreatic tissue can provide valuable confirmation of the diagnosis by highlighting the presence of beta-cell hyperplasia and nesidioblastosis[20], equivalent to the histopathological findings of our case.

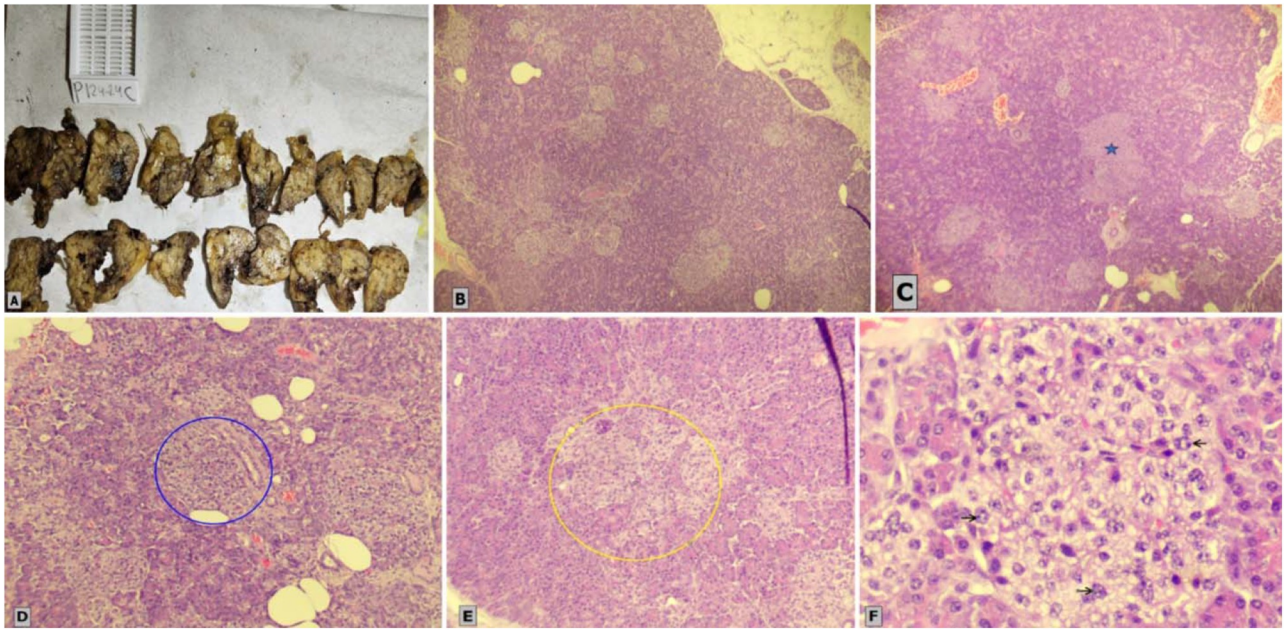

Figure 2. (A) Gross sections of resected distal pancreas. (B) Hematoxylin and eosin H&E staining shows increased numbers of pancreatic islet (x40). (C) H&E staining of islet cells shows variable sizes with irregular borders (blue asterisk) (×40). (D) H&E staining shows intimate relation of islet cells with pancreatic duct (ductuloinsular complexes) (blue circle) (×100). (E) Islet cells arranged in lobules and extending into acini (tubule-insular complex) (yellow circle) (×100). (F) Islet cells exhibit mild nuclear enlargement and irregularity (black arrow) (×400).

A case report by Kim *et al* (2019) presented the first case of nesidioblastosis after sleeve gastrectomy, emphasizing the relationship between incretin physiology and nesidioblastosis[13]. Another study by Service *et al* (2005) reported six patients with postprandial neuroglycopenia after RYGB, histological examination showed nesidioblastosis in all cases, indicating a potential link between gastric bypass surgery and the development of this condition[15]. Cao *et al* (2022) described a 37-year-old woman

Table 2

Key differences between nesidioblastosis, post-bariatric hypoglycemia syndrome, and dumping syndrome

Feature	Nesidioblastosis	PBHS	Dumping syndrome
Prevalence	Extremely rare	Occurs in 0.1–34% of post-bariatric surgery patients	Common in patients with rapid gastric emptying
Sleeve versus RYGB	RYGB > Sleeve		
Pathophysiology	β -cell hyperplasia and hypertrophy stimulated by GLP-1, GIP, and IGF-2	Excessive insulin release triggered by altered incretin patterns	Rapid gastric emptying with altered nutrient absorption
Timing of symptoms	Postprandial	1–3 hours Postprandial	Early or late postprandial
Symptoms	Hypoglycemia, blurred vision, tremors, altered consciousness	Hypoglycemia, disorientation, fatigue, autonomic and neuroglycopenic symptoms	Nausea, abdominal discomfort, diarrhea, flushing, palpitations, tachycardia
Definitive diagnosis	Histopathological findings: β -cell hyperplasia and ductuloinsular complexes	Incretin response evaluation	Clinical and imaging evidence
Diagnostic challenges	Normal imaging findings, requires histopathological confirmation	Mixed-meal tolerance test, glucose monitoring	Clinical evaluation, gastric emptying studies
Glucose patterns	Persistent hypoglycemia	Fluctuating glucose levels with exaggerated insulin response	Initial hyperglycemia followed by hypoglycemia (late dumping)
Hormonal markers	Elevated insulin, C-peptide; absence of tumor markers	Altered incretin hormone levels (e.g., elevated GLP-1)	Not typically associated with significant hormone changes
Onset timing post-surgery	Often months to years post-surgery	Usually months post-surgery	Can occur within weeks of surgery
Treatment	Surgical intervention for refractory cases	Dietary modifications, medications (e.g., acarbose)	Dietary changes, symptomatic management
Surgical indicators	Required in refractory cases with histopathological confirmation	Rarely requires surgery	Surgery is not typically indicated

PBHS, post-bariatric hypoglycemia syndrome; RYGB, Roux-en-Y gastric bypass.

with severe hypoglycemia resistant to standard treatment; a gallium-68 advanced PET scan localized nesidioblastosis lesion, and resection resolved symptoms, emphasizing advanced imaging's role[17].

Management of nesidioblastosis post-RYGB involves initially dietary modifications and medical therapy such as acarbose, octreotide, and glucagon, Similar to dumping syndrome and post-bariatric hypoglycemia, however, some patients such as our case do not respond to medical treatment and require surgical intervention[18]. Surgical options include partial or subtotal pancreatectomy, which has been shown to alleviate hypoglycemic symptoms in refractory cases. The choice of surgical approaches, such as laparoscopic or robotic pancreatectomy, may depend on the extent of pancreatic involvement and the patient's overall condition[19,21]. In our case, subtotal pancreatectomy provided resolution of our patient's hypoglycemia and post-surgical pathology confirmed the diagnosis of nesidioblastosis.

It is essential to differentiate between dumping syndrome, post-bariatric hypoglycemia, and nesidioblastosis because, although they have similar symptoms, their pathophysiologies and management approaches are different (Table 2). Nesidioblastosis can result in chronic hypoglycemia and potentially fatal complications if it is misdiagnosed as post-bariatric hypoglycemia or late dumping syndrome[15]. Additionally, unnecessary surgical procedures may be prevented if the condition is detected at an early stage. Admitting these differences is important for adjusting treatment according to the cause and ensuring the best outcomes for patients, especially in uncommon conditions such as nesidioblastosis[17].

Due to the rarity of nesidioblastosis, it is recommended to undertake long-term monitoring to confirm the resolution of symptoms and to identify any possible recurrence of hypoglycemia. Further research is needed to explain the exact pathogenesis of nesidioblastosis and to establish less invasive diagnostic and therapeutic options. A multidisciplinary approach, involving endocrinologists, surgeons, and pathologists, is essential for achieving optimal patient outcomes.

Conclusion

This case highlights the importance of recognizing nesidioblastosis as a cause of persistent hypoglycemia, especially in patients with history of bariatric surgery. Early recognition, comprehensive diagnostics, and a multidisciplinary approach are essential for effective management. While surgical intervention remains the definitive treatment for such cases, future research should explore non-invasive diagnostic techniques and alternative therapies to enhance patient care and outcomes.

Ethical approval

As it's a case report, it is exempted from ethical approval by local institution responding on the case (Ibn-sina Hospital, Jenin, Palestine).

Consent

Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author's contribution

H.A.A., K.R., L.M., W.A., and M.M.: study concept and data collection; H.A.A., K.R., and A.S.: writing the manuscript; H.A. A. and M.M.: review & editing the manuscript; L.M.: imaging interpretation.

Conflicts of interest disclosure

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Data availability statement

The data is available upon reasonable request.

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