Clinical and Experimental Gastroenterology

Dovepress
Taylor & Francis Group

Open Access Full Text Article

CASE REPORT

Clinically Adult-Onset Nesidioblastosis with Repeated Severe Hypoglycemia, Successfully Treated by Two Times Pancreatectomies. A Rare Case Report

Wataru Izumo[1], Ryota Higuchi[1], Masahiro Shiihara[1], Shuichiro Uemura[1], Takehisa Yazawa[2], Noriyoshi Takano[3], Atsuhiro Ichihara[3], Toru Furukawa[4], Yoji Nagashima[5], Masakazu Yamamoto[2], Goro Honda[1]

[1]Department of Surgery, Institute of Gastroenterology, Tokyo Women's Medical University, Shinjuku-ku, Tokyo, Japan; [2]Gastrointestinal Surgery, Utsunomiya Memorial Hospital, Utsunomiya, Tochigi, Japan; [3]Department of Endocrinology and Hypertension, Tokyo Women's Medical University, Shinjuku-ku, Tokyo, Japan; [4]Department of Investigative Pathology, Tohoku University Graduate School of Medicine, Aoba-ku, Sendai, Japan; [5]Department of Surgical Pathology, Tokyo Women's Medical University, Shinjuku-ku, Tokyo, Japan

Correspondence: Wataru Izumo, Department of Surgery, Institute of Gastroenterology, Tokyo Women's Medical University, 8-1 Kawada-cho, Shinjuku-ku, Tokyo, 162-8666, Japan, Tel +81 3 3353 8111, Fax +81 3 5269 7507, Email izumo.wataru@twmu.ac.jp

Abstract: Although nesidioblastosis is the most common cause of hyperinsulinemic hypoglycemia in infants, it is rare in adults. Nesidioblastosis is pathologically characterized by diffuse neoformation of the islets of Langerhans islets from the pancreatic ductal epithelium and is a disease that does not exhibit neoplastic proliferation, unlike insulinoma. Hence, we present a rare case of adult-onset nesidioblastosis that caused repeated severe hypoglycemic symptoms and was cured by pancreatic resection twice, resulting in total pancreatectomy. A 37-year-old woman with the Whipple's triad visited our institution. In the fasting test, the plasma glucose level decreased and immunoreactive insulin levels increased after 12 h. No tumor was identified in the pancreas by imaging. A selective arterial calcium injection test revealed that step-up was detected only in the gastroduodenal artery. The patient underwent pancreatoduodenectomy with a diagnosis of adult-onset nesidioblastosis, with the pancreatic head region as the culprit. Pathological examination revealed neither tumorous islet cells nor an obvious increase in the number of islets. However, there were some isolated single insulin-producing cells in the pancreatic parenchyma, which could cause hyperinsulinemia and hypoglycemia. This patient was diagnosed with adult-onset nesidioblastosis. After the operation, the hypoglycemic symptoms improved, but 1 year later, the same symptoms recurred. The patient underwent remnant pancreatectomy and had no hypoglycemic symptoms for > 5 years after the second surgery.

Keywords: nesidioblastosis, adult, pancreatectomy, repeat

Introduction

Nesidioblastosis is the most common cause of hyperinsulinemic hypoglycemia in infants but is extremely rare in adults.[1,2] Insulinoma is the most frequent cause of hyperinsulinemic hypoglycemia in adult.[2] Nesidioblastosis is pathologically characterized by diffuse neoformation of the islets of Langerhans islets from the pancreatic ductal epithelium, a disease that does not exhibit neoplastic proliferation, unlike insulinoma.[3] While insulinomas can be identified with various imaging modalities, adult-onset nesidioblastosis is difficult to detect using imaging modalities.[4–7] To diagnose adult-onset nesidioblastosis, it is necessary to suspect the disease based on clinical findings, endocrine examinations, and imaging studies and then perform a selective arterial calcium injection (SACI) test.[8–13] The present study describes a rare case of adult-onset nesidioblastosis in a patient with heterochronic repeated severe hypoglycemic symptoms that was cured by pancreatic resection twice, resulting in total pancreatectomy.

Received: 8 February 2025
Accepted: 2 July 2025
Published: 8 July 2025

Case Report

A 37-year-old woman was referred to our hospital with complaints of weight loss (height: 160.4 cm, weight dropped from 90 to 66 kg in half a year) and repeated disturbances of consciousness. She was diagnosed with manic depression at a previous hospital. She had Whipple's triad but did not take oral hypoglycemic agents or receive insulin injection therapy. She had no medical or family history of endocrine-related diseases including insulinoma, diabetes mellitus, or multiple endocrine neoplasia type 1.

Laboratory data showed that the serum levels of fasting plasma glucose (PG), immunoreactive insulin (IRI), connecting peptide immunoreactivity (CPR), and hemoglobin A1c, and a urine levels of CPR were 31 mg/dl, 11.6 μU/mL, 6.6 mg/mL, 5.2%, and 115.2 μg/day, respectively. Fajan's index (IRI / PG), Grunt's index (PG / IRI), and Turner's index [(IRI × 100) / (PG - 30)] were 0.37, 2.7, 1160, respectively (Table 1a). In the fasting test, the PG level was decreased to 45 mg/dl and IRI was increased to 10.0 μU/mL after 12 hours (Table 1b). In the octreotide loading test, the PG level was increased to 155 mg/dl after 120 minutes and IRI was decreased to 0.3 μU/mL after 30 minutes (Table 1c). Antiinsulin antibodies were absent. The function and imaging studies of the pituitary, adrenal, parathyroid, and thyroid glands were within normal limits. On imaging studies, including ultrasonography, contrast-enhanced computed tomography, magnetic resonance imaging, and endoscopic ultrasonography, no tumor was identified in the pancreas (Figure 1). In addition, upper gastrointestinal endoscopy and colonoscopy revealed no findings in the gastrointestinal tract, suggesting ectopic insulinoma. The SACI test revealed that step-up was detected only in the gastroduodenal artery (GDA) and not in the proper hepatic, splenic, and superior mesenteric arteries (Figure 2).

Based on the above examination results, the patient was clinically diagnosed with adult-onset nesidioblastosis originating from the pancreatic head. Initially, she was treated with diazoxide (300 mg, taken daily) for 1 months; however, but symptoms of impaired consciousness persisted. Subsequently, she received octreotide acetate therapy (30mg, once every 4 weeks; Sandostatin LAR; Novartis, Basel, Switzerland) and had no hypoglycemic symptoms for 1 year. However, the patient subsequently experienced relapse of hypoglycemic symptoms. The patient's home blood glucose levels were not measured. The results of the SACI test were the same as the previous time, with a step-up only in the GDA, and no tumor was detected in the imaging studies. She underwent pancreatoduodenectomy for adult-onset nesidioblastosis with the pancreatic head region as the culprit, which was poorly controlled with drug therapy.

Pathological examination of the resected pancreas revealed no neoplastic proliferation of pancreatic β-cells, or an obvious increase in the size or number of islets. Immunohistochemical examination revealed numerous isolated insulin-

Table 1 Endocrine Examinations

a) Index of insulin secretion						
	Calculation methods				**Results**	
Fajan's index Grunt's index Turner's index	IRI / PG PG / IRI (IRI × 100) / (PG - 30)				0.37 2.7 1160	
b) Fasting test						
Time (hour)	**0**		**6**		**12**	
PG (mg/dl) IRI (μU/mL) CPR (ng/mL)	102 30.2 4.3		87 3.9 1.5		45 10.0 2.3	
c) Octreotide loading test						
Time (minute)	**0**	**30**	**60**	**120**	**240**	**360**
PG (mg/dl) IRI (μU/mL)	61 6.6	82 0.3	114 0.4	155 2.2	140 3.2	103 4.2

Abbreviations: PG, fasting plasma glucose; IRI, immunoreactive insulin; CPR, connecting peptide immunoreactivity.

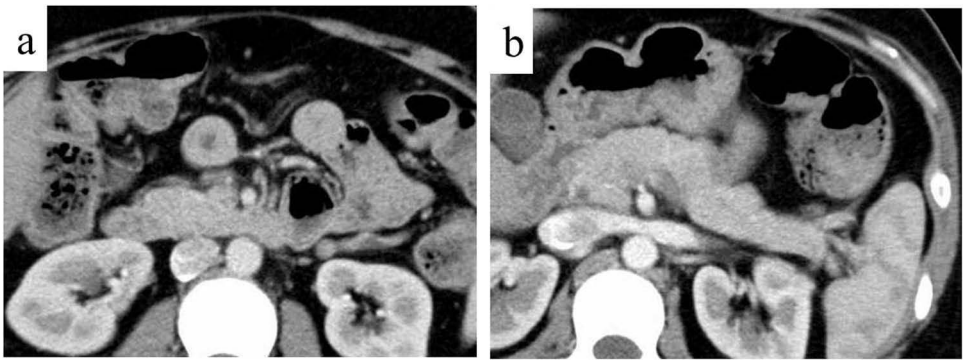
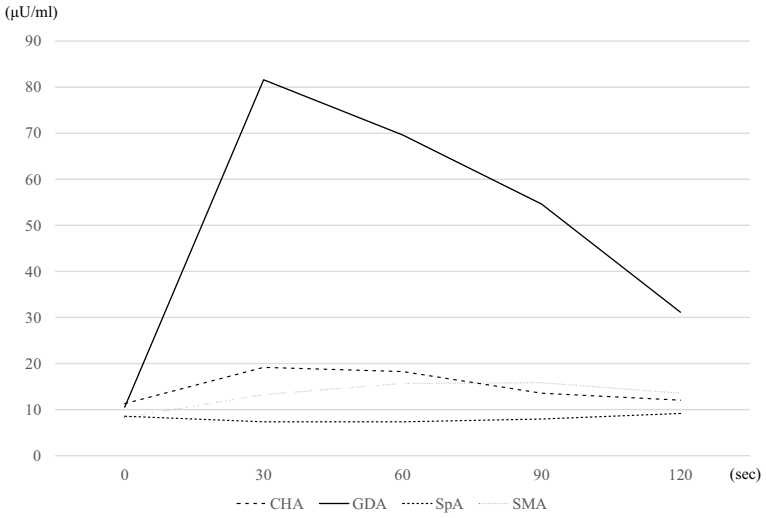


Figure 1 Contrast-enhanced computed tomography at initial diagnosis. There were no tumorous lesions from pancreatic uncus to head (**a**) and from pancreatic body to tail (**b**) on contrast-enhanced computed tomography.



	Time (sec)	0	30	60	90
	Selective artery				
Insulin (μU/ml)	CHA	11.3	19.1	18.3	13.5
	GDA	10.6	81.6	69.7	54.7
	SpA	8.6	7.4	7.3	8.0
	SMA	8.2	13.3	15.7	15.8

Figure 2 The results of selective arterial calcium injection test. The serum level of insulin status based on a selective arterial calcium injection test SACI (Calcium gluconate hydrate: 0.025 mEq/kg injection).
Abbreviations: SACI, selective arterial calcium injection; CHA, common hepatic artery; GDA, gastroduodenal artery; SpA, splenic artery; SMA, superior mesenteric artery.

producing cells in the pancreatic parenchyma. Therefore, insulinoma was not thought to be the cause of the hypoglycemia in this patient. The numerous isolated insulin-producing cells in the pancreatic parenchyma may have caused the hyperinsulinemia and hypoglycemia in this patient (Figure 3). Although the patient pathologically did not fully meet the diagnostic criteria for nesidioblastosis, she was clinically diagnosed with adult-onset nesidioblastosis. After the first operation, the hypoglycemic symptoms disappeared; however, 1 year later, she gradually complained of the same symptoms. Therefore, the patient underwent remnant total pancreatectomy for heterochronic recurrent adult-onset nesidioblastosis, with the remnant pancreas as the responsible lesion. The resected remnant pancreas showed the same pathological features as those of the preceding pancreatectomy specimen, with no islet tumors but numerous isolated insulin-producing cells in the parenchyma (Figure 4). After the second surgery, the patient had no hypoglycemic symptoms for > 5 years (Figure 5). However, seven years later, the patient died of sepsis due to Fournier's gangrene.

https://doi.org/10.2147/CEG.S520986

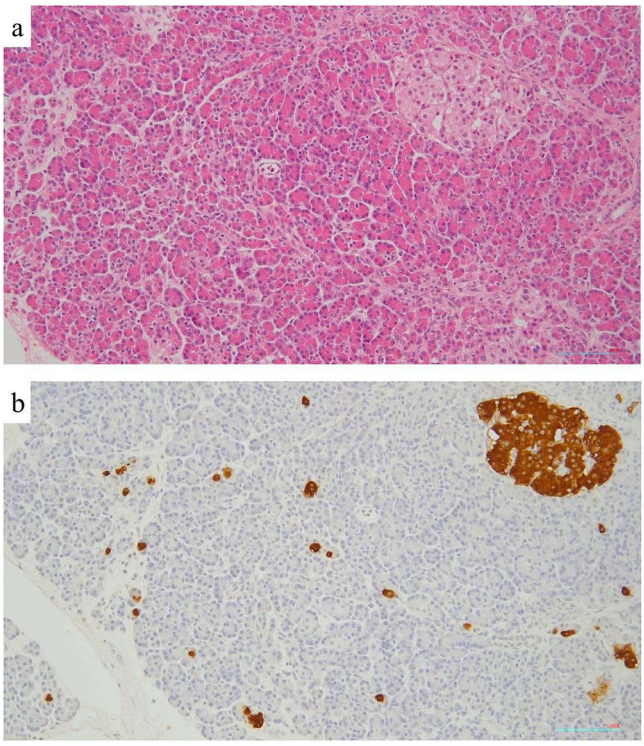


Figure 3 Histopathological findings of resected specimen at the first surgery. (**a**) On hematoxylin and eosin staining of the resected pancreas, there were no neoplastic proliferation of pancreatic beta cells and increasing in the number or size of pancreatic islet cells. (**b**) On immunostaining staining for insulin of the resected pancreas, there were numerous isolated insulin-producing cells in the pancreatic parenchyma.

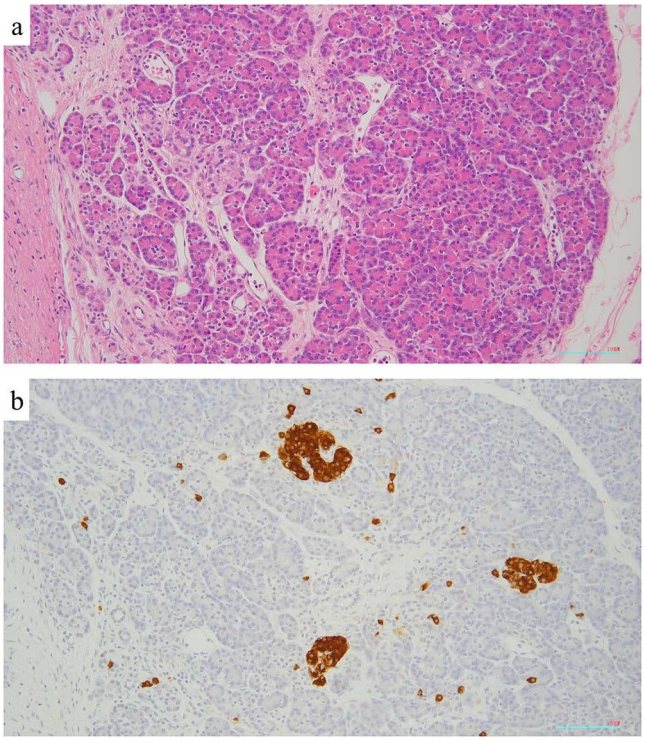


Figure 4 Histopathological findings of resected specimens at the second surgery. (**a**) On hematoxylin and eosin staining, tumorous proliferation of pancreatic beta cells and increasing in the number or size of pancreatic islet cells failed to show. (**b**) On immunostaining staining for insulin of resected pancreas, there were numerous isolated insulin-producing cells in the pancreatic parenchyma.

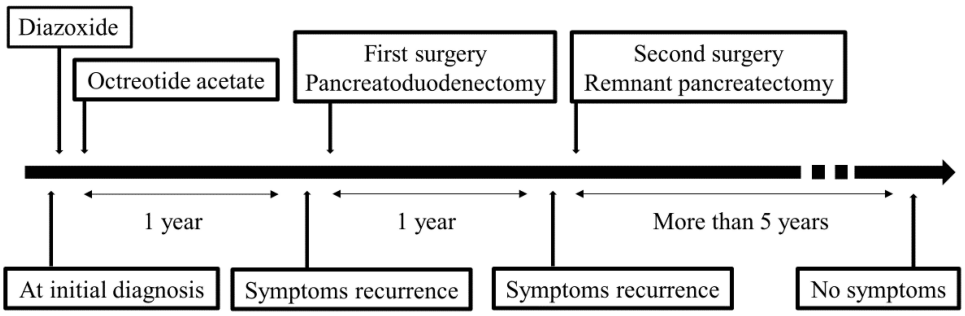


Figure 5 Clinical course. Initially, she was treated with diazoxide for 1 months. However, symptoms of impaired consciousness persisted. Subsequently, she received octreotide acetate therapy and had no hypoglycemic symptoms for 1 year. However, the patient subsequently experienced relapse of hypoglycemic symptoms. She underwent pancreatoduodenectomy. One year later, she gradually complained of the same symptoms. Therefore, the patient underwent remnant total pancreatectomy. After the second surgery, the patient had no hypoglycemic symptoms for > 5 years.

Discussion

There are a wide variety of diseases that cause consciousness disturbance and weight loss, including endocrine and psychiatric diseases; however, hypoglycemia due to hyperinsulinemia is also an important differential diagnosis. Causes of hyperinsulinemic hypoglycemia include such as insulinoma, insulin autoimmune syndrome, the use of insulin secretagogues, and nesidioblastosis.[1,2,14] Nesidioblastosis, first named by Laidlaw in 1938,[3] has been reported to cause intractable hypoglycemia due to the diffuse proliferation of pancreatic beta cells. Nesidioblastosis is a disease characterized by severe postprandial hypoglycemia and hyperinsulinemia unresponsive to dietary therapy, and its mechanism is characterized by an abnormal increase in β-cell mass and diffuse neoformation of the islets of Langerhans islets from the pancreatic ductal epithelium.[3] Though, nesidioblastosis is recognized as the most common cause of hyper-insulinemic hypoglycemia in infants, it is very rare in adults, and the first adult case of nesidioblastosis has been reported in 1975.[1,2,15] In an epidemiological survey conducted in Japan from 2017 to 2018, 205 cases of insulinoma were reported, of which 95% were aged 20 years or older, whereas only 9 cases of nesidioblastosis occurred in patients aged 20 years or older.[16] In recent years, adult-onset nesidioblastosis has also been reported after gastric bypass surgery for bariatric surgery and gastrectomy with Roux-en-Y anastomosis,[17] these conditions are now collectively described as non-insulinoma pancreatogenous hypoglycemia syndrome.[18] However, the developmental mechanism of adult-onset nesidioblastosis remains unclear, and several causes have been speculated, including dysregulation of beta cell function,[19] increased production of growth factors,[20] and unidentified genetic mutations.[21] In recent years, mutations have been identified in several β-cell genes involved in insulin secretion, the most common of which are in the ABCC8 or KCNJ11 genes. A better understanding of the functions of these genes may help elucidate the pathogenesis of nesidioblastosis.[22] Conversely, insulinoma is the most common cause of hyperinsulinemic hypoglycemia in adults and a rare disease in infants.[1,2] In both diseases, it is important to first diagnose the existence of hypoglycemia due to hyperinsulinemia and then determine the localization of the responsible lesion. Whipple's triad is a classical feature of hyper-insulinemic hypoglycemia.[8] In addition, insulin secretion indices using PG and IRI, such as Fajan's, Grunt's, and Turner's indices, fasting test, and octreotide loading test, are helpful in the initial diagnosis.[9–12] Misdiagnosis of nesidioblastosis as a psychiatric disorder is likely to delay appropriate treatment and result in detrimental effects on the patient's quality of life. This patient had repeated disturbances of consciousness, but was misdiagnosed with manic depression. In this case, the patient had Whipple's triad, and all indices except Grunt's index met the diagnostic criteria for hyperinsulinemic hypoglycemia. Although the sensitivity and specificity of these tests are not sufficient,[23] it is clinically important to consider that the positive results of these tests can raise suspicions about nesidioblastosis or insulinoma. In addition, hypoglycemia results in various symptoms, including confusion, loss of consciousness, and seizures, so when these symptoms appear, it is necessary to consider whether hypoglycemia and the hyperinsulinemia that causes it may be the underlying cause.

A definitive diagnosis of nesidioblastosis was made postoperatively, based on histopathological findings. Pathological criteria have been proposed for the diagnosis of adult-onset nesidioblastosis, and consist of four major criteria and some minor criteria.[24] The four major criteria are as follows. First, insulinomas were excluded by macroscopic, microscopic, and immunohistochemical examination. Second, there were multiple β-cells with enlarged hyperchromatic nuclei and

 https://doi.org/10.2147/CEG.S520986

abundant clear cytoplasms. Third, islet cells have a normal spatial distribution among the different cell types. Finally, there is no endocrine cell proliferation activity. The identification of a ductuloinsular complex, characterized by the neoformation of islet cells arising from the pancreatic ductal epithelium, is also conclusive evidence of nesidioblastosis. However, as in this case, some cases do not completely meet these pathological criteria but show clinically similar symptoms, and the pathogenesis of adult-onset nesidioblastosis has not yet been fully established. In contrast, insulinomas are characterized by neoplastic proliferation of pancreatic beta cells.[4] Therefore, insulinoma is typically identified as a hypervascular tumor in imaging studies, whereas nesidioblastosis cannot be detected on imaging studies. The localized diagnostic accuracy of insulinoma by ultrasonography, computed tomography, magnetic-resonance imaging, endoscopic ultrasonography, and somatostatin receptor scintigraphy was reported to be 60–95% and With a recent advances in diagnostic technologies, a high pretreatment diagnostic rate for insulinoma has been reported by combining these imaging modalities.[8–13] The SACI test is an existing and localized diagnosis using insulin secretion function and plays an extremely important role in identifying the region responsible for hyperinsulinemic hypoglycemia.[13] The SACI test involves selective arteriography of the gastroduodenal, splenic, superior mesenteric, and hepatic arteries, and insulinomas are identified using tumor-enhancing staining. Calcium was injected into each artery (0.025 mEq/kg body weight) to assess endocrine function, and insulin was sampled from a catheter placed in the hepatic vein. When an insulinoma or nesidioblastosis is present, calcium injection releases insulin and decreases PG levels only if the specific artery that feeds the area of the pancreas containing these diseases is tested. In the SACI test, blood vessels with plasma insulin levels that were more than double the basal level after calcium injection were considered positive. In this case, the step-up was initially confirmed only in the GDA region; therefore, it was determined that the region responsible for hyperinsulinemia was in the pancreatic head. Therapeutic strategies for nesidioblastosis include pancreatectomy and drug therapy, and the former is considered as the optimal and curative treatment.[25,26] It has also been reported that a high-carbohydrate diet with appropriate protein adjustment and reduced fat intake is effective in controlling of hypoglycemia in patients with nesidioblastosis;[27] however, it has also mentioned that although these medications and dietary therapies have reduced severe hypoglycemic episodes, manageable hypoglycemic episodes still occur.[27] In nesidioblastosis, partial pancreatic resection may cause continuous hypoglycemic symptoms, whereas total pancreatectomy leads to insulin-dependent diabetes mellitus. It has been reported, including in this case, that hyperinsulinemic hypoglycemia recurs over time after the culprit lesion is removed, but the mechanism is still unclear. Therefore, it may be important to continue follow-up for the recurrence of hypoglycemic symptoms after surgery. Recently, nesidioblastosis due to pancreatic islet hyperplasia after gastric Roux-en-Y bypass surgery has been reported,[17] and this may help elucidate the changes that occur in the remnant pancreas over time after the initial pancreatectomy. Previous literatures suggested that when the disease persists, a 70–90% resection of the pancreatic tissue is advisable in order to avoid the possibility of developing post-operative diabetes and cure the hyperinsulinemic hypoglycemia.[25,26] We believe that adult-onset nesidioblastosis might improve if the responsible region is removed. Since total pancreatectomy eliminates the exocrine and endocrine functions of the pancreas, various complications may occur after surgery. When we searched for the keyword "nesidioblastosis, adult, total pancreatectomy" in PubMed, three case reports were found.[28–30] The age at the time of total pancreatectomy ranged from 22 to 32 years, and all the patients were women. Two cases with records of treatment history were similar to this case in that they had undergone two-stage total pancreatectomy.[28,29] One of these was a report of pyoderma gangrenosum after total pancreatectomy due to nesidioblastosis.[30] Therefore, in our opinion, regional pancreatectomy should be performed for the responsible lesion initially rather than total pancreatectomy, and secondly to remnant pancreatectomy if hyperinsulinemic hypoglycemia symptoms reappear during the post-operative period. In adult-onset nesidioblastosis, in which hypoglycemia cannot be controlled by subtotal pancreatectomy or drug therapy, total pancreatectomy may be a treatment option given the current advances in insulin preparations and pancreatic enzyme replacement therapy. However, in such cases, it is important to ensure that patients fully understand the importance of continuing the diabetes treatment.

In patients who did not show normalization of glycemia by surgery or did not undergo pancreatectomy, chronic use of somatostatin analogs, diazoxide, or verapamil hydrochloride has been reported.[31,32] Diazoxide is a frequently used drug for nesidioblastosis; however, it has some adverse effects, including fluid retention, hypotension, hypertrichosis, and bone marrow suppression.[31] However, these treatments are primarily aimed at palliating the symptoms rather than curatively.

In this case, diazoxide did not improve the symptoms; therefore, the patient was promptly transferred to the next treatment. Although octreotide acetate therapy was subsequently able to alleviate the symptoms to a certain extent, the control worsened over time; therefore, surgical resection was selected.

Conclusion

In conclusion, the present study reports a case of heterochronic adult-onset nesidioblastosis that was cured twice with pancreatectomy, resulting in total pancreatectomy. When an adult patient presents with repeated hypoglycemic symptoms and insulinoma cannot be identified on imaging, adult-onset nesidioblastosis should be considered as a differential diagnosis. It is important to perform an existing and localized diagnosis, treat the responsible lesion, and be mindful of the possibility of recurrence in the residual pancreas.

Ethics Statement

Written informed consent was obtained from the patient for the publication of this report and accompanying images prior to death. Institutional ethics committee approval was not required to publish this manuscript. All procedures were performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Goudswaard WB, Houthoff HJ, Koudstaal J, Zwierstra RP. Nesidioblastosis and endocrine hyperplasia of the pancreas: a secondary phenomenon. *Hum Pathol*. 1986;17(1):46–54. doi:10.1016/S0046-8177(86)80154-X
2. Jabri AL, Bayard C. Nesidioblastosis associated with hyperinsulinemic hypoglycemia in adults: review of the literature. *Eur J Intern Med*. 2004;15(7):407–410. doi:10.1016/j.ejim.2004.06.012
3. Laidlaw GF. Nesidioblastoma, the islet tumor of the pancreas. *Am J Pathol*. 1938;14:125–134.
4. Doherty GM, Doppman JL, Shawker TH, et al. Results of a prospective strategy to diagnose, localize, and resect insulinomas. *Surgery*. 1991;110:989—97.
5. Noone TC, Hosey J, Firat Z, Semelka RC. Imaging and localization of islet—cell tumors of the pancreas on CT and MRI. *Best Pract Res Clin Endocrinol Metab*. 2005;19:195—211.
6. Khashab MA, Yong E, Lennon AM, et al. EUS is still superior to multidetector computerized tomography for detection of pancreatic neuroendocrine tumors. *Gastrointest Endosc*. 2011;73(4):691–696. doi:10.1016/j.gie.2010.08.030
7. Ito T, Hijioka S, Masui T, et al. Advances in the diagnosis and treatment of pancreatic neuroendocrine neoplasms in Japan. *J Gastroenterol*. 2017;52(1):9–18. doi:10.1007/s00535-016-1250-9
8. Whipple AO, Frants VK. Adenoma of islet cells with hyperinsulinism. A review. *Ann Surg*. 1935;101:1299–1335. doi:10.1097/00000658-193506000-00001
9. Fajans SS, Floyd JC. Fasting hypoglycemia in adults. *New Engl J Med*. 1976;294:766–772. doi:10.1056/NEJM197604012941408
10. Grunt JA, Pallota JA, Soeldner JS. Blood sugar, serum insulin and free fatty acid interrelationships young adults and patients with insulinomas. *Diabetes*. 1970;19:122–126. doi:10.2337/diab.19.2.122
11. Turner RC, Oakley NW, Nabarro JDN. Control of basal insulin secretion, with special reference to the diagnosis of insulinomas. *Br Med J*. 1971;2:132–135. doi:10.1136/bmj.2.5754.132
12. Cryer PE, Axelrod L, Grossman B, et al. Evaluation and management of adult hypoglycemic disorders: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2009;94(3):709–728. doi:10.1210/jc.2008-1410
13. Doppman JL, Chang R, Fraker DL; SACI test, et al. Localization of insulinomas to regions of the pancreas by intraarterial stimulation by calcium. *Ann Intern Med*. 123;1995:269–273. doi:10.7326/0003-4819-123-4-199508150-00004
14. Hirata Y, Ishizu H, Ouchi N. Insulin autoimmunity in a case of spontaneous hypoglycemia. *J Jpn Diabetes Soc*. 1970;13:312–320.
15. Sandler R, Horwitz DL, Rubenstein AH, Kuzuya H. Hypoglycemia and endogenous hyperinsulinism complicating diabetes mellitus. *Am J Med*. 1975;59730–59736.

16. Yamada Y, Kitayama K, Oyachi M, et al. Nationwide survey of endogenous hyperinsulinemic hypoglycemia in Japan (2017–2018): congenital hyperinsulinism, insulinoma, non-insulinoma pancreatogenous hypoglycemia syndrome and insulin autoimmune syndrome (Hirata's disease). *J Diabetes Investig*. 2020;11(3):554–563. doi:10.1111/jdi.13180
17. Service GJ, Thompson GB, Service FJ, Andrews JC, Collazo-Clavell ML, Lloyd RV. Hyperinsulinemic hypoglycemia with nesidioblastosis after gastric-bypass surgery. *N Engl J Med*. 2005;353(3):249–254. doi:10.1056/NEJMoa043690
18. Service FJ, Natt N, Thompson GB, et al. Noninsulinoma pancreatogenous hypoglycemia: a novel syndrome of hyperinsulinemic hypoglycemia in adults independent of mutations in Kir6.2 and SUR1 genes. *J Clin Endocrinol Metab*. 1999;84(5):1582–1589. doi:10.1210/jcem.84.5.5645
19. Dravecka I, Lazurova I. Nesidioblastosis in adults. *Neoplasma*. 2014;61:252–256. doi:10.4149/neo_2014_047
20. Rumilla KM, Erickson LA, Service FJ, et al. Hyperinsulinemic hypoglycemia with nesidioblastosis: histologic features and growth factor expression. *Mod Pathol*. 2009;22:239–245. doi:10.1038/modpathol.2008.169
21. Klöppel G, Anlauf M, Raffel A, Perren A, Knoefel WT. Adult nesidioblastosis: genetically or environmentally induced? *Hum Pathol*. 2008;39:3–8. doi:10.1016/j.humpath.2007.09.010
22. Sempoux C, Klöppel G. Pathological features in non-neoplastic congenital and adult hyperinsulinism: from nesidioblastosis to current terminology and understanding. *Endocr Relat Cancer*. 2023;30(9):e230034. doi:10.1530/ERC-23-0034
23. Service FJ. Hypoglycemic disorders. *N Eng J Med*. 1995;332:1144–1152. doi:10.1056/NEJM199504273321707
24. Anlauf M, Wieben D, Perren A, et al. Persistent hyperinsulinemic hypoglycemia in 15 adults with diffuse nesidioblastosis: diagnostic criteria, incidence, and characterization of beta-cell changes. *Am J Surg Pathol*. 2005;29(4):524–533. doi:10.1097/01.pas.0000151617.14598.ae
25. Witteles RM, Straus FH, Sugg SL, Koka MR, Costa EA, Kaplan EL. Adult-onset nesidioblastosis causing hypoglycemia: an important clinical entity and continuing treatment dilemma. *Arch Surg*. 2001;136:656–663. doi:10.1001/archsurg.136.6.656
26. Valli V, Blandamura S, Pastorelli D, Merigliano S, Sperti C. Nesidioblastosis coexisting with non-functioning islet cell tumour in an adult. *Endokrynol Pol*. 2015;66(4):356–360. doi:10.5603/EP.2015.0045
27. Barsi Á, Beke A, Sármán B. Case report: a particularly rare case of endogenous hyperinsulinemic hypoglycemia complicated with pregnancy treated with short-acting somatostatin analog injections. *Front Endocrinol*. 2022;15(13):964481. doi:10.3389/fendo.2022.964481
28. Darawsha B, Agbaria A, Stein P, Khuri S. Nesidioblastosis in pregnancy: navigating the diagnostic and therapeutic challenges of a rare condition. *Cureus*. 2024;16(10):e71985. doi:10.7759/cureus.71985
29. Soares F, Providência R, Pontes M. Nesidioblastosis: an undescribed cause of transient loss of conscience in young adults. *Europace*. 2013;15 (10):1506. doi:10.1093/europace/eut033
30. Lemos AC, Aveiro D, Santos N, Marques V, Pinheiro LF. Pyoderma gangrenosum: an uncommon case report and review of the literature. *Wounds*. 2017;29(9):E61–E69.
31. Herder WW, Niederle B, Scoazec JY, et al. Well—differentiated pancreatic tumor carcinoma: insulinoma. *Neuroendocrinology*. 2006;126:183–188. doi:10.1159/000098010
32. Usukura M, Yoneda T, Oda N, et al. Medical treatment of benign insulinoma using octreotide LAR: a case report. *Endocr J*. 2007;54:95—101. doi:10.1507/endocrj.K05-157