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Case Report

# Complex glycemic instability in a patient with nesidioblastosis: diagnostic and therapeutic challenges

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## Abstract

Diffuse congenital hyperinsulinism (CH) can be resistant to medical therapy and may require total pancreatectomy. This procedure controls hypoglycemia but frequently results in pancreatogenic diabetes (type 3c) and persistent exocrine insufficiency, creating significant management challenges. A 14-year-old female with a family history of CH and recurrent hypoglycemia since infancy was initially treated with diazoxide (15 mg/kg/day) and high-carbohydrate intake, which failed. She underwent subtotal pancreatectomy at age 3, without improvement. A total pancreatectomy at age 5 led to insulin-dependent diabetes. She was managed with conventional insulin (1 U/kg/day), pancreatic enzyme replacement (Creon 7,500 U/kg/day), and fat-soluble vitamins (A, D, E, K). At age 14, she presented with poorly controlled diabetes (HbA1c 12.6%) characterized by unstable glycemia and frequent severe hypoglycemia despite insulin analogues. She also had steatorrhea (5 greasy stools/day; 13 g/24 h) without other signs of malabsorption. Laboratory results were within normal limits for calcium, potassium, and hemoglobin. No micro- or macrovascular complications were observed. Management included insulin dose adjustment, optimization of pancreatic enzymes, and continuation of vitamin supplementation. Pancreatogenic diabetes after total pancreatectomy for diffuse CH requires individualized, multidisciplinary management. Careful optimization of insulin therapy, pancreatic enzyme replacement, and vitamin supplementation is essential to achieve metabolic stability, prevent hypoglycemia, and maintain nutritional status.

**Keywords:** pancreatogenic diabetes, total pancreatectomy, congenital hyperinsulinism, nesidioblastosis

## Introduction

Pancreatogenic diabetes, also known as type 3c diabetes mellitus (T3cDM), is a distinct yet often underrecognized form of diabetes resulting from pancreatic disease or surgery. Unlike type 1 or type 2 diabetes, T3cDM arises from the combined loss of both insulin-producing β-cells and glucagon-secreting α-cells, leading to profound disturbances in glucose regulation and frequent episodes of hypoglycemia [1].

This complex endocrine dysfunction often occurs in the context of exocrine pancreatic insufficiency, further complicating management through malabsorption, steatorrhea, and deficiencies in fat-soluble vitamins [2]. Patients frequently experience wide glycemic fluctuations due to the absence of counterregulatory hormones and impaired nutrient absorption, making insulin therapy particularly challenging [3].

We report the case of a 14-year-old female with congenital hyperinsulinism due to nesidioblastosis who underwent total pancreatectomy and subsequently developed pancreatogenic diabetes. The case illustrates the therapeutic and metabolic challenges of managing brittle diabetes in a patient with complete loss of pancreatic endocrine and exocrine function.

## Case presentation

A 14-year-old female with a family history of congenital hyperinsulinism (CH), including an elder sister who died at 18 months, presented with a history of

recurrent hypoglycemia since infancy. She had been hospitalized in pediatrics for refractory hypoglycemia, with hyperinsulinemia (203 pmol/L) during hypoglycemic episodes, suggestive of nesidioblastosis.

Initial management included diazoxide (15 mg/kg/day) and high daily carbohydrate intake. Due to persistent hypoglycemia with seizure episodes, she underwent a subtotal pancreatectomy at age 3, which failed to resolve symptoms. She was also treated with valproate (Depakine).

A diffuse diazoxide-resistant form of CH was suspected. At age 5, the patient underwent a total pancreatectomy, resulting in insulin-dependent diabetes (pancreatogenic diabetes, type 3c according to ADA). Postoperatively, she was managed with conventional insulin therapy (1 U/kg/day), pancreatic enzyme replacement therapy (Creon 7,500 U/kg/day), and fat-soluble vitamin supplementation (A, D, E, K).

She was admitted to our service for poorly controlled diabetes (HbA1c 12.6%), characterized by unstable glycemia with frequent severe hypoglycemic episodes despite insulin analogues. The patient also exhibited steatorrhea (5 greasy stools/day; 13 g/24 h) without other clinical or laboratory signs of malabsorption. Laboratory values showed normal calcium (2.5 mmol/L), potassium (4.7 mmol/L), and hemoglobin (14 g/dL). No microvascular or macrovascular complications were noted.

Management involved reduction of insulin doses, optimization of pancreatic enzyme supplementation, continuation of fat-soluble vitamin therapy, and follow-up for steatorrhea monitoring.

## Discussion

Pancreatogenic diabetes (T3cDM) is a secondary form of diabetes resulting from pancreatic disease, including total pancreatectomy, leading to both endocrine and exocrine pancreatic insufficiencies. This condition presents unique management challenges due to the combined loss of insulin and glucagon secretion, as well as impaired nutrient absorption.

Post-pancreatectomy, patients often exhibit brittle diabetes characterized by significant glycemic variability and frequent hypoglycemic episodes. This instability arises from the loss of glucagon secretion, which impairs counterregulatory responses to hypoglycemia [1]. Insulin therapy is essential, but careful dosing is required to balance hyperglycemia and hypoglycemia risks. Studies have shown that insulin requirements in T3cDM patients can be lower than those in type 1 diabetes, possibly due to residual pancreatic function or differences in insulin sensitivity [2].

Exocrine pancreatic insufficiency is common in T3cDM, leading to malabsorption, steatorrhea, and deficiencies in fat-soluble vitamins (A, D, E, K). Pancreatic enzyme replacement therapy is crucial for managing EPI and preventing malnutrition [3, 4]. Adequate enzyme dosing is necessary to achieve optimal nutritional status and support metabolic control [5].

Fat-soluble vitamin deficiencies are prevalent due to impaired absorption. Supplementation with vitamins A, D, E, and K is recommended to prevent associated complications, such as bone disease and coagulopathy [6, 7]. Regular monitoring of vitamin levels is essential to adjust supplementation appropriately [8].

The complexity of T3cDM necessitates a multidisciplinary approach, involving endocrinologists, gastroenterologists, dietitians, and other healthcare professionals [9]. Regular monitoring of glycemic control, nutritional status, and vitamin levels is essential for optimizing patient outcomes. Personalized treatment plans should be developed to address the unique needs of each patient [10].

## Conclusion

Pancreatogenic diabetes following total pancreatectomy for diffuse congenital hyperinsulinism presents significant management challenges, including unstable glycemia, frequent hypoglycemia, and persistent exocrine insufficiency. Careful adjustment of insulin therapy, pancreatic enzyme replacement, and vitamin supplementation is essential to achieve metabolic control and prevent long-term complications. Early recognition and multidisciplinary management are crucial for optimal outcomes.

## Conflict of interest

The authors declare no conflict of interest.

## Consent to participate

Written informed consent was obtained from the participant.


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