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ORIGINAL RESEARCH

Reclassification of Diabetes Types in Post Pancreatitis Patients- A Case Series Demonstrating the Importance of Thorough Evaluation for Optimal Treatment

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ABSTRACT

Background: Diabetes following pancreatitis, often termed post pancreatitis diabetes, poses diagnostic and therapeutic challenges. Accurate classification of diabetes among post pancreatitis patients is crucial for tailoring appropriate treatment approaches. Despite meeting criteria for pancreatic diabetes, some patients may benefit from reevaluation due to evolving clinical presentations and diagnostic advancements. This case series highlights the significance of meticulous evaluation in reclassifying different types of diabetes among post pancreatitis patients to optimize treatment strategies. We present three cases where patients initially diagnosed with pancreatic diabetes and treated with insulin were reclassified as other types of diabetes, leading to improved response to oral glucose-lowering therapy. **Methods:** Three cases of post pancreatitis diabetes initially managed as pancreatic diabetes but reclassified based on thorough clinical, biochemical, and radiological assessments were presented. Detailed clinical histories, physical examinations, laboratory investigations, and imaging findings were documented to elucidate the reclassification process. **Results:** Case 1 involves a 25-year-old male with acute hepatic encephalopathy and newly diagnosed diabetes. After reclassification as T2DM, he responded positively to oral glucose-lowering agents. Case 2 involves a 55-year-old female with chronic calcific pancreatitis and T3C Diabetes Mellitus. Hypercalcemia due to parathyroid adenoma led to reclassification as T2DM and successful transition to OAD therapy. Case 3 involves a 25-year-old female with psoriasis vulgaris and chronic steroid therapy. **Conclusion:** This case series underscores the importance of comprehensive evaluation in reclassifying post pancreatitis diabetes, as illustrated by diverse clinical presentations and responses to treatment. Clinicians should consider reevaluation in patients with atypical features or inadequate response to initial therapy to ensure optimal diabetes management post-pancreatitis.

Keywords: Post pancreatitis diabetes, chronic pancreatitis, diabetes mellitus classification, insulin therapy, oral glucose lowering therapy.

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder causing hyperglycemia due to defects in insulin secretion or action. Pancreatic diabetes, particularly post pancreatitis, presents unique diagnostic and management challenges. Chronic pancreatitis, characterized by inflammation and fibrosis, can lead to complications like pancreatic diabetes. The pancreas plays a crucial role in glucose homeostasis through insulin production and secretion, and any disruption can result in diabetes. Diabetes is categorized into type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM), gestational diabetes mellitus (GDM), and other specific types. Post pancreatitis diabetes, also known as type 3c diabetes mellitus (T3cDM), accounts for a significant proportion of secondary diabetes cases[1]. Classifying and managing diabetes among post pancreatitis patients is crucial for optimizing treatment strategies and improving patient outcomes[2].

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Chronic pancreatitis is a progressive inflammatory disorder of the pancreas characterized by irreversible destruction of pancreatic tissue, fibrosis, and ductal abnormalities. It can lead to various complications, including pancreatic exocrine and endocrine insufficiency, pseudocysts, pancreatic ascites, and pancreatic cancer[3]. Pancreatic diabetes, as a consequence of chronic pancreatitis, accounts for a significant proportion of secondary diabetes cases[4].

The exact prevalence of post pancreatitis diabetes is challenging to determine due to variations in study populations, diagnostic criteria, and methods of assessment. However, studies have reported a prevalence ranging from 5% to 50% among patients with chronic pancreatitis, depending on the severity and duration of the disease[5]. Post pancreatitis diabetes is more common in individuals with alcoholic pancreatitis compared to other etiologies[6].

Post pancreatitis diabetes is a condition characterized by multiple mechanisms, including pancreatic endocrine and exocrine dysfunction, pancreatic inflammation, fibrosis, and alterations in pancreatic polypeptide secretion. Chronic pancreatitis leads to the destruction of pancreatic beta cells, resulting in impaired insulin secretion and glucose dysregulation. Pancreatic exocrine insufficiency, often observed in chronic pancreatitis, impairs the release of incretin hormones and affects glucose metabolism. Chronic inflammation and fibrosis can also lead to alterations in the microenvironment, affecting islet cell function and survival[7,8].

Post pancreatitis diabetes shares clinical features with other types of diabetes, making diagnosis challenging. Patients may present with classic diabetes symptoms, but concurrent pancreatic exocrine insufficiency can manifest as steatorrhea, abdominal pain, and malnutrition. Patients with post pancreatitis diabetes may have a history of chronic pancreatitis or pancreatic surgery, alcohol abuse, or other risk factors[9].

Diagnosis of post pancreatitis diabetes requires a high index of suspicion, especially in patients with a history of chronic pancreatitis or pancreatic surgery. Current diagnostic criteria for post pancreatitis diabetes are based on clinical judgment, laboratory investigations, and imaging findings suggestive of pancreatic pathology. However, these criteria lack sensitivity and specificity, leading to potential misdiagnosis or underdiagnosis[10].

Management of post pancreatitis diabetes involves addressing both pancreatic endocrine and exocrine dysfunction, optimizing glycemic control, and managing complications of chronic pancreatitis. Treatment strategies may include lifestyle modifications, pharmacological therapy, pancreatic enzyme replacement therapy (PERT), and surgical interventions[11].

JUSTIFICATION

The case series highlights the importance of accurate diagnosis and classification in treating patients with chronic pancreatitis. It highlights the challenges in distinguishing post pancreatitis diabetes from other types of diabetes based on clinical features, laboratory investigations, and imaging findings. The heterogeneity of diabetes among post pancreatitis patients necessitates individualized management approaches. Accurate classification of diabetes can guide treatment decisions, improve glycemic control, and reduce the risk of complications associated with misdiagnosis or inappropriate management. Post pancreatitis diabetes is a unique subtype of diabetes mellitus characterized by pancreatic endocrine and exocrine dysfunction. Understanding the epidemiology, pathophysiology, clinical features, diagnostic challenges, and management considerations of post pancreatitis diabetes is crucial for selecting appropriate treatment strategies and optimizing patient outcomes.

LEARNING OBJECTIVES

1. To explore the significance of accurately classifying diabetes among post-pancreatitis patients to tailor treatment approaches effectively.
2. To identify the diverse clinical presentations of diabetes in individuals with a history of pancreatitis, including altered sensorium, polyuria, steatorrhea, and other associated symptoms.
3. To recognize the diagnostic challenges posed by post-pancreatitis diabetes, including distinguishing it from other types of diabetes and managing associated complications such as hepatic encephalopathy and hypercalcemia.

CASE PRESENTATION

CASE 1

A 25-year-old male presented to the Emergency Department with altered sensorium. He had a history of yellowish discoloration of the eyes and native medicine intake. Over the past 10 days, he experienced polyuria and steatorrhea. Notably, he had no prior history of diabetes, hypertension, or pancreatitis, and no family history of Type 2 diabetes mellitus.

Upon physical examination, his body mass index was 29 kg/m², blood pressure measured 100/50 mmHg, heart rate was 120 beats/min, and respiratory rate was 22/min. Icterus was observed along with mild hepatomegaly, extensor plantar response, and asterixis. Investigations revealed deranged liver function tests, high plasma glucose, positive urine ketones, and acidosis on arterial blood gas analysis. Contrast-enhanced computed tomography (CECT) showed hepatomegaly with evidence of acute on chronic pancreatitis with a pseudocyst. A diagnosis of acute hepatic encephalopathy with acute on chronic calcific pancreatitis and newly diagnosed diabetes

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mellitus was established, initially managed as T3c Diabetes Mellitus.

Further investigation revealed negative autoimmune markers and high C-peptide values after achieving good glycemic control. Subsequently, the patient was reclassified as T2DM and showed a favorable response to oral glucose-lowering agents.

CASE 2

A 55-year-old female presented to our Outpatient Department with complaints of polyuria, generalized malaise, and steatorrhea persisting for the past 2 months. She had a known case of chronic calcific pancreatitis and was previously diagnosed with T3c Diabetes Mellitus requiring insulin therapy. Physical examination revealed no signs of insulin resistance, and her BMI was 23.7 kg/m².

Investigations demonstrated elevated plasma glucose levels exceeding 400 mg/dL, along with hypercalcemia. Urinary ketones were negative. CECT revealed evidence of chronic calcific pancreatitis alongside multiple renal calculi. Further investigation for hypercalcemia revealed elevated parathormone levels, indicative of parathyroid adenoma. Consequently, the patient underwent bilateral parathyroidectomy.

Subsequent investigations revealed negative autoimmune markers and high C-peptide values, prompting the reclassification of diabetes as T2DM. She responded well to oral glucose-lowering agents.

CASE 3

A 25-year-old female, known for psoriasis vulgaris for 15 years and chronic steroid therapy, presented to our OPD with elevated blood sugars and steatorrhea. She had a history of acute pancreatitis 1 year ago, following which diabetes was diagnosed and managed as T3cDM. The patient was referred to our OPD for glycemic control.

Physical examination revealed a BMI of 26 kg/m² without signs of insulin resistance. CECT revealed chunky calcification of the pancreas suggestive of chronic calcific pancreatitis. Her plasma glucose remained persistently elevated without ketosis. Given her clinical phenotype, further evaluation led to the reclassification of diabetes as T3eDM. She was subsequently treated with oral antidiabetic agents.

Table1: Summary of case details

	Age/ Gender	Poly's wt loss	Family history	BMI	Signs of IR	Admitting sugar S	Ketoacidosis	Alcoholic	DM Duration	Abnormal pancreatic imaging	Exocrine insufficiency	Antibodies		C-peptide(0.5-3ng/ml)		Final diagnosis
												Gad>5U/ml	IA2>7.5U/ml	Fasting	Stimualted	
Sulochana	55/F	++/++	No	23.7	Nil	>3000	No	No	Recently Diagnosed	CCp	Present	4.8	4	1.7	2.5	T2DM

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Santhiya	25/F	No	Father	26	Fatty liver	>400	No	No	1 year	CCP	Present	5	4	0.9	1.7	T3eDM
Mohan	25/M	+/-	No	29	Acanthosis/fatty liver	DKA>400	Yes	5 yrs	Recently Diagnosed	Acute on CP	Present	4	5	0.5	0.7	T2DM

REVIEW OF LITERATURE

1. *Amandeep et al*[12] discusses post-pancreatitis diabetes mellitus (PPDM), which has become the second most common cause of new-onset diabetes in adults, surpassing type 1 diabetes. Despite this, there is a lack of understanding among practitioners regarding its diagnosis and management. The authors aim to address this gap by providing a brief review on the risks, diagnosis, and management of PPDM, with a focus on dietary and lifestyle strategies. They emphasize the importance of a team-based approach involving gastroenterologists, endocrinologists, primary care physicians, nutritionists, and behavioral health specialists in managing PPDM effectively. Additionally, they highlight that new-onset diabetes in pancreatitis patients may also indicate an underlying pancreatic malignancy.
2. The study by *Viggers et al*[13] examined the prescription patterns of glucose-lowering therapy in patients with postpancreatitis diabetes mellitus (PPDM) compared to type 1 and type 2 diabetes. It was found that a significant proportion of patients with PPDM were misclassified as having type 2 diabetes and prescribed medications potentially harmful for PPDM. Conversely, many patients with PPDM did not receive medications associated with improved outcomes for the condition. Insulin requirements were higher in patients with PPDM compared to type 2 diabetes, particularly in cases associated with chronic pancreatitis. These findings highlight the need for proper classification and management of PPDM, which differs from type 2 diabetes.
3. The article by *Hart et al*[14]discusses diabetes mellitus that arises following acute pancreatitis, termed pancreatogenic or type 3c diabetes. It explores the epidemiology, pathophysiology, and management of this condition, highlighting the complexity and knowledge gaps surrounding its development. The pathophysiology of acute pancreatitis-related diabetes mellitus is not fully understood, but it is believed to be multifactorial. The article emphasizes the need for further research to better understand and manage this complication of acute pancreatitis.
4. This review by *Richardson et al*[15] examines the association between acute pancreatitis (AP) and diabetes mellitus (DM), particularly focusing on type 3c diabetes mellitus (T3cDM). T3cDM, resulting from AP, has distinct pathophysiology, affecting disease progression and treatment. Studies indicate that around 15% of individuals develop DM within 1 year post-AP, with increasing rates over 5 years. Some experience transient hyperglycemia post-AP, with a subset developing persistent impaired glucose metabolism. Risk factors for post-AP DM are unclear, but AP severity may play a role. Screening guidelines post-AP are lacking, but screening at 1 year may identify newly developed DM. Dysfunction of both endocrine and exocrine pancreas is observed post-AP, suggesting a close link. Additionally, there is evidence suggesting DM predisposes individuals to pancreatic structural changes and increased AP risk.
5. The article by *Petrov et al*[16] discusses post-pancreatitis diabetes mellitus (PPDM), a type of secondary diabetes resulting from pancreatitis. Despite being less common than type 2 diabetes, PPDM is increasingly recognized due to recent studies. Individuals with pancreatitis have a significantly higher risk of developing diabetes, particularly after acute or chronic pancreatitis episodes. Recurrent pancreatitis and exocrine pancreatic dysfunction increase the risk, especially in young or middle-aged non-obese men. PPDM is associated with poorer glycemic control, higher cancer risk (especially pancreatic cancer), younger age at death, and increased mortality compared to type 2 diabetes. Metformin is recommended as first-line therapy for PPDM. Early screening, accurate diagnosis, and

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appropriate management are crucial to improving outcomes for this significant secondary disease.

DISCUSSION

The presented cases shed light on the challenges and importance of accurate classification in managing diabetes among patients with chronic pancreatitis. The pathophysiology of T3cDM involves progressive destruction of pancreatic beta cells due to chronic inflammation and fibrosis in the pancreas[17]. This is consistent with findings in the presented cases, where patients exhibited evidence of chronic pancreatitis on imaging studies, further complicated by additional factors such as acute exacerbations and comorbidities.

Previous studies have elucidated the complex interplay between pancreatic endocrine and exocrine dysfunction in T3cDM, emphasizing the importance of considering both aspects in diagnosis and management[18,19]. In Case 1, the patient presented with acute hepatic encephalopathy alongside newly diagnosed DM, underscoring the multisystem involvement and diagnostic challenges in T3cDM.

The cases highlight the diagnostic challenges of post pancreatitis diabetes, emphasizing the importance of a comprehensive evaluation. This is consistent with previous studies that have reported the difficulty in distinguishing post pancreatitis diabetes from other types of diabetes based on clinical presentation alone[20]. The variability in symptoms and overlapping features with other types of diabetes necessitates a multifaceted approach to diagnosis, incorporating clinical judgment, laboratory investigations, and imaging findings[2].

Reclassification of diabetes subtype based on further investigation and response to treatment underscores the dynamic nature of diabetes management. Our findings align with previous studies that have demonstrated the potential for reclassification of diabetes subtype among post pancreatitis patients[14]. The ability to accurately classify diabetes enables tailored treatment approaches, leading to improved glycemic control and patient outcomes.

Imaging modalities such as CECT play a crucial role in diagnosing pancreatitis and assessing pancreatic pathology. Our cases demonstrate the utility of CECT in identifying pancreatic calcifications and pseudocysts, aiding in the diagnosis of post pancreatitis diabetes. This is consistent with previous studies highlighting the importance of imaging in evaluating pancreatic pathology and guiding treatment decisions[3].

While our cases primarily focus on reclassifying post pancreatitis diabetes as T2DM, previous studies have highlighted the heterogeneity of diabetes subtypes among post pancreatitis patients. Some patients may present with features consistent with other specific types of diabetes, such as latent autoimmune diabetes in adults (LADA) or pancreatogenic diabetes[2]. This variability underscores the need for individualized management approaches based on the underlying pathophysiology and clinical presentation.

The etiology of pancreatitis, whether alcoholic or non-alcoholic, may influence the clinical course and management of post pancreatitis diabetes. While our cases do not specifically address the etiology of pancreatitis, previous studies have suggested differences in the prevalence and severity of post pancreatitis diabetes based on etiology[4]. Alcoholic pancreatitis, for instance, may be associated with a higher risk of diabetes and pancreatic exocrine insufficiency compared to other etiologies.

CONCLUSION

The presented cases underscore the challenges in diagnosing and managing type 3c diabetes mellitus (T3cDM) secondary to chronic pancreatitis. These cases highlight the importance of a comprehensive evaluation, including clinical history, physical examination, and ancillary tests, for accurate diagnosis and classification. Furthermore, the cases demonstrate the evolving nature of T3cDM diagnosis, with potential reclassification based on changing clinical parameters. Individualized treatment approaches tailored to the underlying pathophysiology and patient preferences are essential for optimizing outcomes. Multidisciplinary collaboration is key for comprehensive patient care. Future research should focus on validating findings, exploring novel diagnostic biomarkers, and assessing therapeutic interventions to improve T3cDM management.

RECOMMENDATIONS

The findings from our cases have several implications for clinical practice and future research. Firstly, they emphasize the importance of a holistic approach to the evaluation and management of post pancreatitis diabetes, taking into account not only biochemical parameters but also clinical phenotype and response to treatment. This underscores the need for multidisciplinary collaboration involving endocrinologists, gastroenterologists, and imaging specialists to optimize patient care.

Secondly, the cases Diabetologist, endocrinologist, gastroenterologist subtype based on individual patient characteristics and treatment response. Future research exploring the predictive factors for treatment response and long-term outcomes following reclassification may further refine our understanding of post pancreatitis diabetes and inform personalized treatment strategies.

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