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Case Report

Diabetes as an Initial Presentation of Intraductal Papillary Mucinous Neoplasm

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Abstract

This is a case of an older man with no prior history of diabetes presenting with a combination of diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) in the setting of new-onset diabetes mellitus. His further work-up revealed intraductal papillary mucinous neoplasm (IPMN) on pancreatic imaging. Though his diabetes etiology could be multifactorial, it is possible that it is an initial presentation of IPMN. Data have been suggestive of diabetes mellitus associated with degree of dysplasia and worse prognosis of IPMN but the exact pathophysiology behind this is unknown, and it is unclear whether diabetes mellitus is an early presentation of IPMN. We discuss possible differential diagnoses needed to evaluate patients for possible triggers behind DKA and etiologies behind new-onset diabetes mellitus when indicated.

Key Words: IPMN, intraductal papillary mucinous neoplasm, diabetes

Abbreviations: BMI, body mass index; CA-19-9, carbohydrate antigen 19-9; DKA, diabetic ketoacidosis; HHS, hyperosmolar hyperglycemic state; IPMN, intraductal papillary mucinous neoplasm; MRI, magnetic resonance imaging.

Introduction

New-onset diabetes in patients without considerable risk factors should be thoroughly evaluated to identify underlying causes, as diabetes could be the initial presentation of conditions like pancreatic cancers. The role of intraductal papillary mucinous neoplasms (IPMNs) in causing diabetes is unknown and requires further study.

Case Presentation

A 67-year-old man with a past medical history of stage IIA to IIB cutaneous T-cell lymphoma, hypertension, and tobacco use disorder presented with altered mental status for 2 days, along with generalized weakness, fatigue, and weight loss for a couple of weeks. He had lost his appetite due to altered taste and thus was primarily consuming sugary juices. He denied any family history of diabetes. His last recorded glycated hemoglobin A_{1c} was 5.7% (normal, <5.7%) 5 years ago, and he denied any prior history of diabetes. He had undergone radiation therapy for his cutaneous T-cell lymphoma 2 years prior.

On initial examination, he appeared to be lethargic but was oriented to self and place. His mucosa was dry, and he exhibited a lean body habitus with evidence of acanthosis nigricans. His body mass index (BMI) was 23 (normal range, 18.5-24.9) on presentation, slightly lower from 24 five years ago. There was no documented recent weight loss in the chart review.

Diagnostic Assessment

Initial laboratory work revealed metabolic acidosis with a pH of 7.14 (normal range, 7.35-7.45) and hyperglycemia with a serum glucose of 1400 mg/dL or 77 mmol/L (normal range, <125 mg/dL) with a hyperosmolarity of 416 mOsm/kg (normal range, 275-295 mOsm/kg), increased β-hydroxybutyrate, and ketonuria indicating a combination of diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS). He was also found to have severe hypernatremia with corrected sodium (Na) of 167 mEq/L (normal range, 135-145 mEq/L), lactic acidosis, and acute kidney injury.

C-peptide was initially low during admission due to glucotoxicity but normalized to 1.86 ng/mL (normal range, 0.5-2.0 ng/mL). A repeat C-peptide 1 month later was higher than normal likely due to his impaired renal functions.

An abdominal ultrasound revealed fatty infiltration of the liver. Carbohydrate antigen 19-9 (CA-19-9) testing was performed as part of the pancreatic cancer work-up and was found to be substantially elevated. Subsequent magnetic resonance imaging (MRI) identified a pancreatic IPMN but no solid malignancy. A follow-up magnetic resonance cholangiopancreatography was recommended in 2 years.

Treatment

The patient's acidosis and hyperglycemia resolved with an insulin drip along with fluid replacement. He was subsequently transitioned to subcutaneous insulin as per protocol. His hypernatremia, likely due to fluid depletion secondary to polyuria from hyperglycemia, gradually resolved as well.

His hospital course was later complicated by an axillary abscess, which was treated with antibiotics and incision and drainage.

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Outcome and Follow-up

After stabilization of his glucose and electrolytes, the patient was discharged home with plans for outpatient follow-up with endocrinology and general surgery.

Discussion

This patient's presentation could have been induced by high carbohydrate intake with possible underlying undiagnosed diabetes. The American Diabetes Association recommends screening overweight adults with risk factors and all adults aged 45 years and older for diabetes every 1 to 3 years [1]. Older adults with hyperglycemia have increased mortality rates as compared to others. Screening for diabetes can prevent not just life-threatening hyperglycemic events such as DKA and HHS but can also reduce long-term macrovascular complications in undiagnosed individuals. Additionally, lifestyle modifications in prediabetic individuals or referral to Diabetes Prevention Programs can help delay the onset of diabetes.

This patient was not obese, but BMI does not provide information regarding adipose deposition around the viscera. Since fatty infiltration of the liver was seen, and he was noted to have acanthosis nigricans on physical examination, insulin resistance is highly suggestive.

As this patient's hospital course was complicated by an abscess, it is also very likely that an underlying infection contributed to his hyperglycemia.

There was a suspicion of pancreatic cancer given the severe hyperglycemia, weight loss, age at presentation, history of tobacco use, and new-onset diabetes, but MRI did not reveal any solid malignancy. Although rare, pancreatic cancer should be considered as an etiology behind new-onset diabetes in high-risk individuals, particularly when diagnosed after age 50. Pancreatic cancer is among the top 5 cancer-related causes of mortality and is often diagnosed at an advanced stage due to late-onset symptoms [2]. In some cases, new-onset diabetes could be the only early clue to diagnosis [3].

This patient was incidentally found to have an elevated CA-19-9 and IPMN on MRI. IPMN is a neoplastic disorder involving pancreatic duct epithelium presenting on a spectrum ranging from an incidental finding to causing obstructive jaundice. The association of IPMNs with diabetes is unclear but data have been suggestive of diabetes being related to the degree of dysplasia [4]. Studies indicate that a higher degree of malignancy and invasiveness is associated with diabetes, but the exact mechanism remains unknown [5]. A similar case in 2016 reported an older woman presenting with antibody-positive type 1 diabetes mellitus who was found to have an intraductal papillary mucinous adenoma on pancreatic biopsy [6].

While the mechanism of IPMN-induced diabetes is not well understood, pancreatic cancers have been linked to insulin resistance. Liu et al [7] studied the intracellular mechanism of insulin resistance in skeletal muscles and found that in patients with pancreatic cancers, insulin resistance results from defects in glycogen synthase activity and increased glycogen phosphorylase activity, leading to impaired glycogen synthesis. No abnormalities at the insulin receptor level were observed.

Given our patient's history of radiation therapy for skin cancer, radiation-induced pancreatic destruction was considered. Animal-based studies suggest pancreatic β-cell destruction, and observational studies have shown that individuals who received radiation therapy in childhood or young adulthood developed diabetes later in life [8]. However, this contrasts with our patient, who received radiation therapy only 2 years prior.

No suspicious medication, including immunosuppressants, antidepressants, hormonal agents, antipsychotics, or protease inhibitors were found in his home medication list. The only chemotherapeutic agent that he previously received was aprepitant, which is not known to cause diabetes or hyperglycemia, while bexarotene has rarely been associated with hyperglycemia.

His autoimmune work-up, including antiglutamic acid decarboxylase (GAD) antibody, was also negative for type 1 diabetes.

This patient may have had undiagnosed, uncontrolled diabetes or diabetes secondary to IPMN. His hyperglycemic state appears to be multifactorial as discussed earlier. As current data are insufficient to confirm IPMN as an etiology behind diabetes, further studies are needed to establish the pathophysiology.

Learning Points

- Patients who are at risk of developing diabetes, such as those with prediabetes, obesity, or older than 30 years, should be screened annually.
- Patients with newly diagnosed diabetes without risk factors should be evaluated for secondary causes.
- Triggers for DKA and HHS, such as infections, illnesses, medication noncompliance, or poorly controlled diabetes, should be identified.

Contributors

All authors contributed to this case report. H.R. and S.A. were directly involved in patient management. K.S. and M.H. reviewed the relevant literature. All authors reviewed and approved the final draft.

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Disclosures

The authors have no conflicts of interest to declare. We certify that the submission is original work and is not under review at any other publication.

Informed Patient Consent for Publication

Signed informed consent obtained directly from the patient.

Data Availability Statement

Original data generated and analyzed for this case report are included in this published article.

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