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When Diabetic Ketoacidosis Reveals Pancreatic Cancer: A Case Report and Literature Review

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Abstract **Case Report**

Pancreatic adenocarcinoma is an aggressive cancer often diagnosed at a late stage. This article highlights an unusual presentation: diabetic ketoacidosis (DKA) as the initial manifestation. We present a clinical case illustrating this association and explore the pathophysiological mechanisms linking new-onset diabetes to pancreatic cancer. We emphasize the importance of a thorough evaluation in the face of unexplained DKA, particularly in patients with no prior history of diabetes, to detect potential pancreatic neoplasia early. The implications for diagnosis, therapeutic management, and research perspectives are discussed.

Keywords: Pancreatic Adenocarcinoma, Diabetic Ketoacidosis (DKA), New-Onset Diabetes, ENDPAC Score.

INTRODUCTION

Pancreatic adenocarcinoma is a particularly aggressive malignancy, generally diagnosed at an advanced stage due to non-specific initial symptoms. This cancer has a dismal prognosis, with a 5-year survival rate of less than 10% [1]. Diabetic ketoacidosis (DKA), a severe metabolic complication typically associated with type 1 diabetes, is rarely reported as the initial manifestation of pancreatic adenocarcinoma. This unusual presentation underscores the complex interaction between diabetes and pancreatic cancer, suggesting underlying pathophysiological mechanisms that warrant exploration [1-3]. Diabetes mellitus is recognized as a risk factor for pancreatic cancer, but recently, particular attention has been focused on new-onset diabetes as a possible precursor sign of this oncological pathology. The appearance of DKA in patients with no history of diabetes or with newly diagnosed diabetes should alert clinicians to the possibility of an underlying pancreatic neoplasm [4, 5].

This article aims to examine current data regarding the association between diabetic ketoacidosis and pancreatic adenocarcinoma, to explore the pathophysiological mechanisms involved, and to discuss the clinical implications for early diagnosis and therapeutic management of these patients.

CASE REPORT

A 43-year-old female patient with no known medical history presented to the emergency department with recent onset polyuria, polydipsia, and jaundice. The family history was unremarkable; she did not consume alcohol or smoke, and she had no long-term medication or self-medication use. The patient described a rapid onset in less than ten days of fatigue and yellowing of the skin and mucous membranes with discolored stools and highly concentrated urine. Clinical examination revealed an afebrile patient with a blood pressure of 130/80 mmHg and a pulse of 71 bpm and a BMI at 32 kg/m^2. Cutaneous examination showed manifest cutaneous-mucosal jaundice. There were no obvious signs of dehydration. Abdominal examination was unremarkable on superficial and deep palpation, with no hepatomegaly or palpable mass. Cardiovascular, pleuro-pulmonary, and neurological examinations were unremarkable. There were no disturbances of vigilance or focal neurological signs.

The fasting blood glucose was 3.93 g/L (21.8 mmol/L). Urinalysis showed glycosuria (+++), ketonuria (+++), proteinuria (++), bilirubinuria (+++) and non-hemolyzed hematuria (++).

Laboratory tests showed: Chloride: 105 mmol/l (reference range: 98-107 mmol/l), potassium: 3.5 mmol/l

(reference range: 3.5-5.1 mmol/l), serum sodium: 142 mmol/l (reference range: 135-145 mmol/l). Liver function tests were significantly elevated: AST 279 U/L (<45 U/L), ALT 332 U/L (<45 U/L), alkaline phosphatase 500 U/L (70-380 U/L), gamma GT >1543 U/L (<45 U/L), as well as a very high direct bilirubin level of 113.15 mg/L (<5 mg/L) and a very high total bilirubin level of 138.94 mg/L (3-17 mg/L). The lipase level was normal at 142 U/L (<190U/L). CA19-9 was markedly elevated at 740 U/ml (normal value < 37 U/ml), and CEA at 150ng/ml (normal value < 5ng/ml).

Viral serology was negative for HIV, hepatitis C, and hepatitis B. These results suggested severe liver involvement requiring urgent medical evaluation.

Abdominal ultrasound showed a liver of normal size and echotexture, dilation of the intra- and extrahepatic biliary tracts, a distended gallbladder with sludge, a spleen of normal appearance, and hypertrophy of the pancreatic head. Both kidneys were of normal size without dilation of the pyelocaliceal system. There was no deep adenopathy or intra-peritoneal effusion.

A diagnosis of decompensated diabetic ketoacidosis was made based on glycosuria, ketonuria, hyperglycemia, and a suggestive clinical context. Management with rehydration and insulin therapy was initiated. Abdomino-pelvic CT scan with contrast revealed a process involving the pancreatic head, encasing the superior mesenteric vein (Figure 1 a, b), with dilation of the common bile duct and intrahepatic biliary tracts (Figure 2 a, b), and liver metastases in segments IV, V, and VII (Figure 3 a, b). A liver biopsy (Figure 4) was performed revealing infiltrating carcinomatous proliferation, consisting of clusters, trabeculae, and glands. Immunohistochemical study showed expression of tumor cells to anti-CK7, CK19, MUC5 and MUC1 antibodies, and no expression to anti-CK20 antibody, concluding with hepatic location of a metastasis from a pancreatic adenocarcinoma.

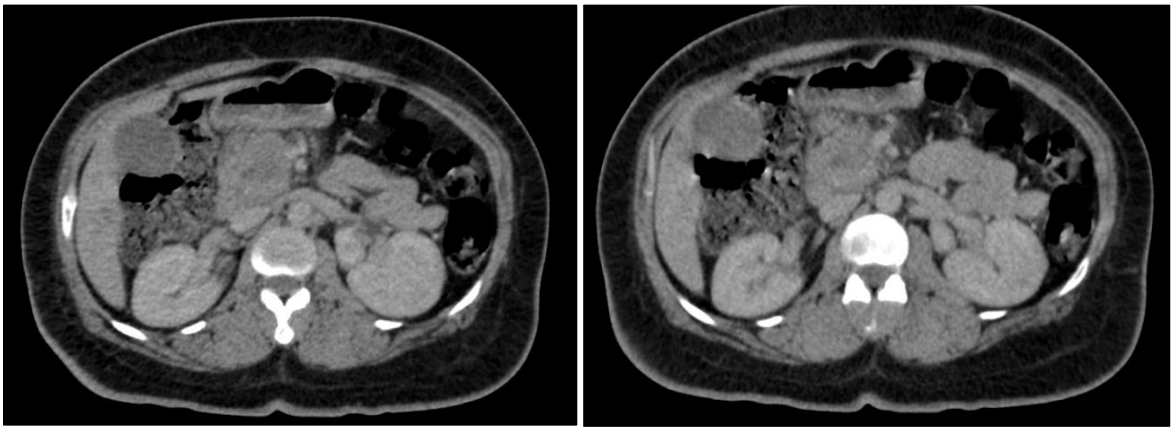

Figure 1: Hypodense lesion of the pancreatic head, encasing the superior mesenteric vein

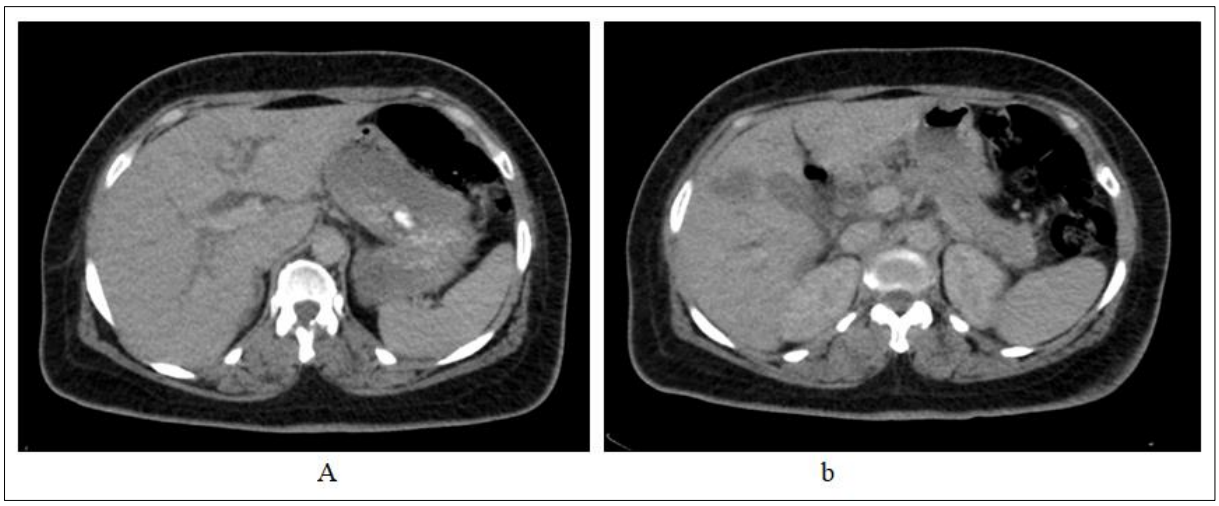

Figure 2: Dilation of the main hepatic bile duct (a) and intrahepatic bile ducts (b)

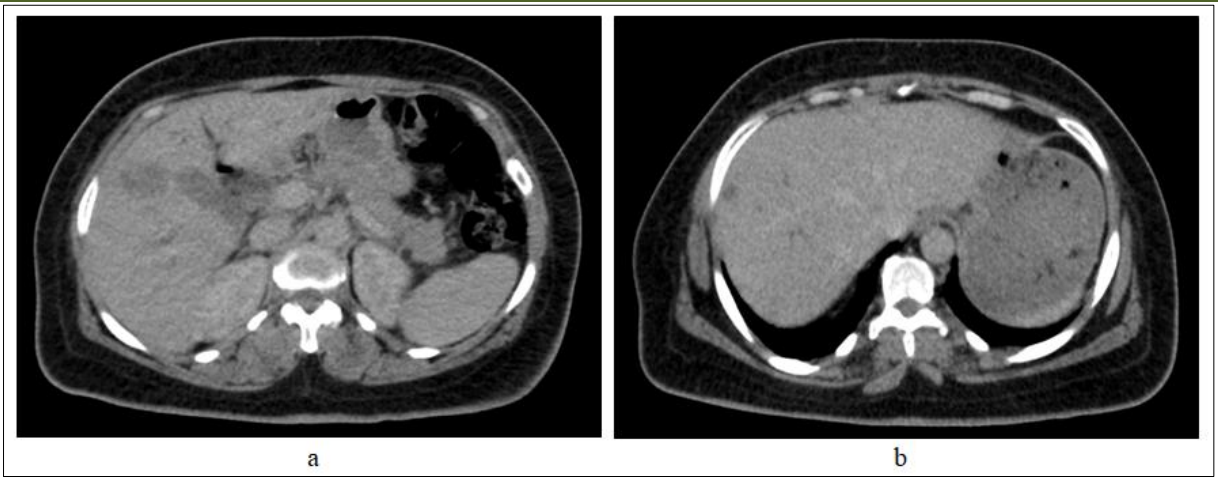

Figure 3: Liver metastases in segments IV and V (a) and VII (b)

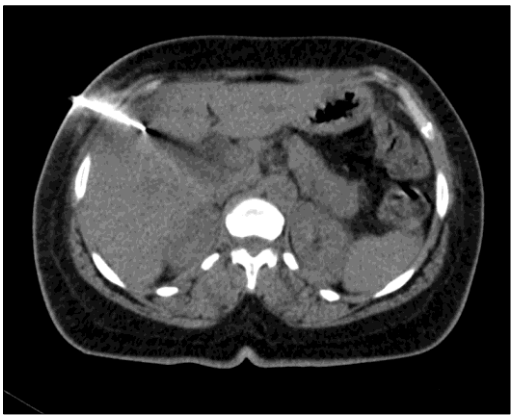

Figure 4: CT-guided liver biopsy

DISCUSSION

Diabetic ketoacidosis (DKA), characterized by hyperglycemia, ketonemia, and metabolic acidosis, primarily results from insulin deficiency and an excess of counter-regulatory hormones. In the context of pancreatic cancer, the onset of DKA can be explained by several mechanisms [1-6]. Pancreatic cancer can induce diabetes in various ways, including altering insulin production through direct destruction of β-cells and inducing insulin resistance through the secretion of pro-inflammatory cytokines and other humoral factors. These metabolic abnormalities can lead to severe hyperglycemia and, in some cases, ketoacidosis [2-7]. Recent studies suggest that certain pancreatic tumors may secrete specific diabetogenic factors, contributing to the onset of diabetes even before the tumor is clinically detectable [4]. The relationship between diabetes and pancreatic cancer is bidirectional and complex. Long-standing diabetes, particularly type 2 diabetes, is an established risk factor for pancreatic cancer, increasing the risk by approximately 1.5 to 2-fold. Conversely, new-onset diabetes in adults over 50 years of age may be an early sign of pancreatic cancer [5-9]. This bidirectional relationship is explained by several mechanisms, including chronic hyperglycemia and hyperinsulinemia, which promote tumor growth via activation of mitogenic signaling pathways. Chronic inflammation associated with diabetes also contributes to pancreatic carcinogenesis, and alterations in the gut microbiota and related metabolic disorders may play a role in tumor progression [7-10].

Although rare, diabetic ketoacidosis can be the initial manifestation of pancreatic adenocarcinoma, as reported in several case studies. Patients typically present with the classic symptoms of DKA: polyuria, polydipsia, dehydration, nausea, vomiting, abdominal pain, and altered mental status [3-11]. It is important to note that this presentation is more common in patients with no history of diabetes or with newly diagnosed diabetes, highlighting the importance of considering an underlying pancreatic neoplasm in these cases [6-12].

In the face of diabetic ketoacidosis in a patient with no prior history of diabetes, particularly in adults over 50 years of age, a thorough diagnostic evaluation is necessary to exclude underlying pancreatic cancer. This evaluation should include a comprehensive laboratory workup, including tumor markers such as CA 19-9 and CEA, and abdominal imaging. Computed tomography (CT) with a pancreatic protocol, endoscopic ultrasound (particularly useful for detecting small lesions), and pancreatic MRI in cases of diagnostic uncertainty are

modalities to be considered. A CT-guided or EUS-guided biopsy may be necessary for histological confirmation [5-13]. The use of the ENDPAC score (enriching new-onset diabetes for pancreatic cancer) has been proposed as a screening tool to identify patients with new-onset diabetes who may benefit from pancreatic cancer screening [5-14].

Initial management of diabetic ketoacidosis in this context follows standard protocols: intravenous rehydration, insulin therapy, correction of electrolyte disorders, and identification and treatment of the underlying cause, which in these cases is pancreatic adenocarcinoma [6-15]. Once the diagnosis of pancreatic adenocarcinoma is established, therapeutic options depend on the stage of the disease and the patient's general condition [16]. Surgery, with pancreatoduodenectomy for resectable tumors, is an option [17]. Chemotherapy, generally based on FOLFIRINOX or gemcitabine-nab-paclitaxel, is also used. Targeted therapies and immunotherapy, including agents such as pembrolizumab, have shown promising results in cases of pancreatic adenocarcinoma with mismatch repair deficiency (MMR), although it may cause immune-related adverse events such as DKA [8]. Management of metabolic complications, including cancer-induced diabetes, is essential. Although the prognosis remains generally poor, early detection through recognition of DKA as a possible initial sign could improve therapeutic outcomes [3].

The rarity of DKA as an initial symptom of pancreatic cancer poses a challenge for early detection. Nevertheless, increased awareness of this association and a systematic consideration of pancreatic cancer in patients presenting with new-onset diabetes and DKA could lead to earlier diagnosis [4]. Current research focuses on the development of more effective blood biomarkers and screening tools to identify at-risk patients. The integration of artificial intelligence into the analysis of clinical and radiological data could also improve early detection [18]. Research is also underway to explore therapeutic interventions targeting the metabolic pathways involved in the relationship between diabetes and pancreatic cancer. The use of natural products and nutritional interventions is being studied as adjunctive treatment to manage diabetes and potentially reduce the risk of cancer [7-9].

CONCLUSION

Diabetic ketoacidosis as an initial presentation of pancreatic adenocarcinoma is a rare, but clinically significant, phenomenon, underscoring the complex relationship between diabetes and pancreatic cancer. This association highlights the importance of a thorough diagnostic approach in patients presenting with DKA without an obvious cause, particularly in those with newly diagnosed diabetes. Early recognition of this association can lead to a faster diagnosis of pancreatic cancer, potentially at a stage where therapeutic options are more effective. A better understanding of the underlying pathophysiological mechanisms could also pave the way for new screening and treatment strategies. A multidisciplinary approach involving oncologists, endocrinologists, radiologists, and surgeons is essential to optimize the management of these complex patients.

Conflicts of Interest:

The authors of this article declare that they have no conflicts of interest. The authors are solely responsible for the information and writing of this article.

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