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New-onset type 2 diabetes mellitus complicated by diabetic ketoacidosis: a sentinel presentation of advanced pancreatic adenocarcinoma

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Summary

Diabetic ketoacidosis (DKA), typically linked to type 1 diabetes or acute illness in type 2 diabetes, can rarely be triggered by pancreatic adenocarcinoma (PA). Though 80% of PA patients have glucose intolerance, DKA is exceptionally uncommon, with fewer than 20 documented cases. A 52-year-old woman with new-onset type 2 diabetes presented with altered mental status, abdominal pain, and 23 kg weight loss over 2 months. Labs confirmed DKA (glucose: 439 mg/dL, pH 7.1, ketonuria). Elevated tumor markers (CA19-9: >10,000 U/mL, CEA: 365 ng/mL) and imaging revealed a 4 cm pancreatic mass with metastases, biopsy-proven as PA. This case underscores PA as a rare but critical DKA precipitant in new-onset diabetes. Unexplained hyperglycemia, rapid weight loss, and markedly elevated tumor markers should prompt malignancy screening. Early multidisciplinary intervention may improve outcomes in this aggressive cancer. Clinicians must maintain high suspicion for occult PA in atypical DKA presentations.

Learning points

- Unexplained weight loss alongside newly-identified type 2 DM warrants thorough evaluation for occult malignancy.
- Elevated CA19-9 and CEA in the context of new-onset diabetes should raise suspicion for pancreatic malignancy.
- DKA may rarely serve as the initial manifestation of pancreatic cancer in newly-identified type 2 DM cases, necessitating a high index of clinical suspicion.

Keywords: pancreatic adenocarcinoma; diabetes; diabetic ketoacidosis; oncology

Background

Diabetic ketoacidosis (DKA), a life-threatening hyperglycemic emergency, is most frequently observed in individuals with type 1 diabetes mellitus (DM) and rarely in type 2 DM. It is classically precipitated by infections, medication nonadherence, or acute physiological stressors such as myocardial infarction or trauma (1). However, emerging evidence suggests that occult malignancies, particularly pancreatic

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adenocarcinoma (PA), may serve as underrecognized triggers for DKA, especially in patients without preexisting diabetes (2, 3). The bidirectional relationship between pancreatic cancer and glucose dysregulation is evident in two key pathways. First, up to 80% of pancreatic cancer patients exhibit new-onset diabetes or impaired glucose tolerance at diagnosis, reflecting cancer-induced metabolic disruption. Conversely, chronic diabetes (≥5 years) independently elevates PA risk by 1.5–2.0-fold, driven by hyperinsulinemia, insulin resistance, inflammation, and IGF-1-mediated pathways. A meta-analysis of 88 studies confirmed this association (RR: 1.94; 95% CI: 1.66–2.27), persisting even after excluding paraneoplastic diabetes. Insulin resistance and chronic hyperglycemia further promote carcinogenesis by activating pancreatic stellate cells and remodeling the extracellular matrix. While new-onset diabetes (≤3 years) often heralds underlying malignancy, long-standing diabetes represents a distinct risk factor, underscoring the bidirectional interplay. Clinicians should thus prioritize vigilant surveillance for pancreatic cancer in patients with chronic diabetes to facilitate early detection and intervention (4, 5, 7, 17, 18, 19, 20).

The mechanisms underlying this phenomenon remain incompletely understood but may involve tumor-induced beta-cell dysfunction, insulin resistance, or paraneoplastic secretion of diabetogenic hormones (6).

PA is notorious for its insidious onset and nonspecific symptoms, often leading to delayed diagnosis and poor prognosis. While weight loss, abdominal pain, and jaundice are hallmark features, metabolic derangements such as hyperglycemia may precede structural tumor detection by months (7). Notably, DKA as the inaugural manifestation of pancreatic cancer is exceedingly rare, with only isolated case reports documenting this association (3, 8, 9, 12, 13, 14, 15).

Here, we present a novel case of a 52-year-old woman with newly-developed type 2 DM, who developed DKA as the initial manifestation of advanced PA. This case amplifies the growing body of evidence that pancreatic malignancy should be considered in patients presenting with DKA, particularly when accompanied by rapid weight loss, new-onset type 2 DM, elevated tumor markers, and imaging abnormalities. Furthermore, it reinforces the importance of early oncologic evaluation in atypical metabolic crises, as timely diagnosis may alter disease trajectory in an otherwise lethal malignancy.

Case presentation

A 52-year-old female patient with a medical history of controlled hypertension, ischemic heart disease, hyperlipidemia, asthma, and newly-developed type 2 DM presented to the emergency department of our medical facility. She reported an unintentional weight loss of 23 kg, decreasing from 98 to 75 kg over the past 2 months. In addition, there was no sign of jaundice or yellowish sclera in our case. Moreover, the family history included hypertension in her mother and sister, gastric cancer in an uncle, and thyroid disease in her mother.

Upon admission, the patient presented with altered mental status and abdominal pain, specifically periumbilical pain that radiated to the flanks. This pain intensified after meals and during sleep. In addition, she reported experiencing polyuria, polydipsia, malaise, anorexia, and a recent onset of fever and chills. Symptoms including flank pain and periumbilical pain were temporarily alleviated by nonsteroidal anti-inflammatory drugs (NSAIDs), particularly by diclofenac sodium.

Two months before this admission, the patient began experiencing progressive abdominal pain, accompanied by weight loss, polyuria, polydipsia, and anorexia. One month earlier, she had been hospitalized for angina and abdominal pain but was discharged with ineffective treatment for asthma. Upon arrival at our medical facility, she presented acutely with decreased consciousness and signs of metabolic decompensation.

Laboratory findings revealed significant hyperglycemia with a fasting blood glucose of 439 mg/dL (normal: 70–100 mg/dL) and HbA1c of 12.3% (normal: <5.7%), accompanied by ketonuria (3+ glucose and 3+ ketones; normal: negative for both) and metabolic acidosis, consistent with DKA. Tumor markers were markedly elevated: CA19-9 exceeded 10,000 U/mL (normal: <37 U/mL), and carcinoembryonic antigen (CEA) was 365 ng/mL (normal: <5 ng/mL for nonsmokers). Hematological analysis demonstrated mild leukopenia (WBC 4,800/μL; normal: 4,000–11,000/μL), elevated C-reactive protein (CRP; normal: <10 mg/L), and severe vitamin D deficiency (25OHD 8.3 ng/mL; normal: 30–100 ng/mL). Liver function tests fell within normal ranges: aspartate aminotransferase (AST) 42 U/L (normal: 8–48 U/L), alanine aminotransferase (ALT) 41 U/L (normal: 7–55 U/L), albumin 3.6 g/dL (normal: 3.5–5.5 g/dL), globulin 2.9 g/dL (normal: 2.0–3.5 g/dL), and total bilirubin 0.7 mg/dL (normal: 0.1–1.2 mg/dL). Pancreatic enzyme levels were notable for amylase at 13 U/L (normal: 30–110 U/L) and lipase at 18 U/L (normal: 13–60 U/L), with amylase below the reference range.

In addition, an infection workup, which included a urine culture and Wright agglutination test, yielded negative results. Diagnostic evaluations included abdominopelvic sonography, which revealed inhomogeneous hepatic parenchyma with hypoechoic lesions suggestive of metastasis and mild right-sided hydronephrosis (Table 1), thus necessitating a computed tomography (CT) scan of abdominopelvic structures.

In terms of therapeutic management, DKA was stabilized through the administration of intravenous fluids, insulin, and electrolyte correction in the emergency department.

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Table 1 Demographic and laboratory tests results obtained from similar reports.

	Reference					
	(2)	(3)	(12)	(13)	(14)	(16)
Gender	Female	Female	Male	Male	Female	Female
Age, years	36	52	70	60	89	48
Co-morbidities	GDM	T2DM*	COPD	T2DM	None	Choledocholithiasis
Family history	Negative	Negative	-	-	Negative	Negative
Alcohol use	No	Yes†	Yes	No	No	No
Smoking	No	No	Yes	Yes	No	No
CA 19-9	30.36	251	60,651	202	>121,000	-
CEA	-	5.5	=	-	3,557	-
CRP	204.27	-	-	-	-	-
WBC	27.95	24.000	11.300	-	-	-
AST	89	98	86	34	479	49
ALT	87	103	617	29	519	79
Lipase	109	1,234	44	-	17	241
Amylase	59	721	-	-	-	-
HbA1c, %	9.7	13.9	-	12.5	14.8	-

T2DM, type 2 diabetes mellitus.
*New onset. †Yes, but stopped 20 years ago.

Following treatment for DKA, the patient was prescribed 22 units of glargine to be administered every night, along with 7 units of Aspart insulin before breakfast, 11 units before lunch, and 6 units before dinner.

The patient was subsequently transferred to the endocrinology department for further evaluation, where pancreatic cancer was suspected based on elevated tumor markers and imaging findings. After a 9-day hospitalization, she was referred to gastroenterology for a malignancy workup, which included an intravenous contrast-enhanced CT scan. This scan report revealed the following: The liver was of normal size, exhibiting coarse density and heterogeneous enhancement, along with multiple hypodense lesions measuring up to 23 × 22 mm in the anterior portion of the left lateral segment and 23 × 23 mm in segment V. These findings are suggestive of multiple metastases with post-treatment changes. In addition, the pancreas displayed a lesion approximately 45 × 40 mm in the body of the pancreas, associated with occlusion of the splenic vein and encasement of the splenic artery, indicative of pancreatic cancer (Fig. 1A, B, C, D). Ultimately, endoscopic ultrasound-guided fine-needle aspiration confirmed the diagnosis of moderately differentiated PA with hepatic metastases (Fig. 2).

Discussion

DKA, a life-threatening complication of DM, is characterized by hyperglycemia, metabolic acidosis, and ketonemia. While commonly precipitated by infections, medication non-adherence, or acute illnesses such as myocardial infarction (1), the patient's presentation of DKA as the initial manifestation of pancreatic malignancy, along with significant weight loss, while also being newly diagnosed with type 2 DM, underscores the importance of considering occult neoplasms in atypical presentations of metabolic crises.

A review of similar cases reveals variability in clinical and laboratory profiles. For example, a 36-year-old

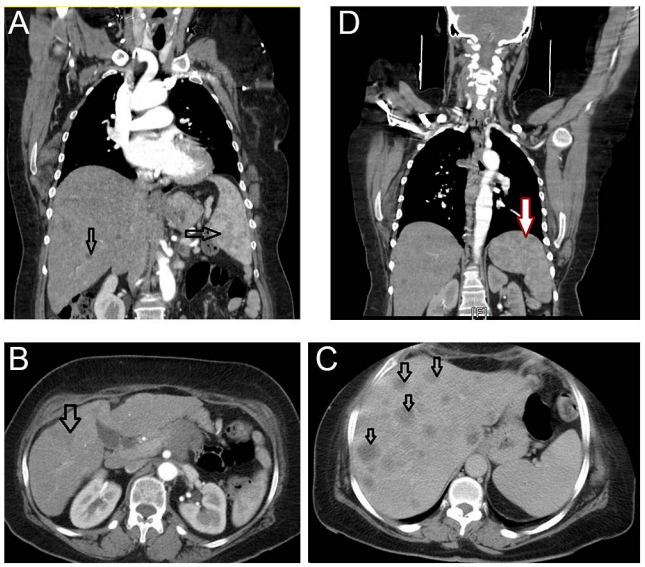

Figure 1

(A, B, C, D) Abdominopelvic computed tomography scan findings: the liver exhibited a normal size, characterized by coarse density and heterogeneous enhancement, with multiple hypodense lesions measuring up to 23 × 22 mm in the anterior portion of the left lateral segment and 23 × 23 mm in segment V, suggestive of multiple metastases with post-treatment changes. In addition, the pancreas presented a lesion approximately 45 × 40 mm in the body of the pancreas, accompanied by occlusion of the splenic vein and encasement of the splenic artery, indicative of pancreatic cancer.

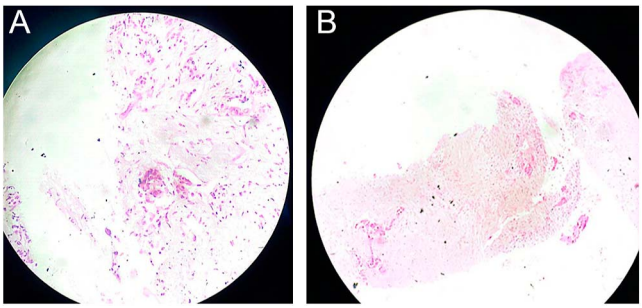

Figure 2

Histopathological examination confirming the PA. (A) the tissue exhibits a prominent desmoplastic stroma characterized by a sparse distribution of neoplastic cells that demonstrate an invasive growth pattern. (B) The neoplastic cells show moderate atypia and nuclear pleomorphism, with clear evidence of perineural invasion.

female with gestational diabetes (2) and a 52-year-old female with new-onset type 2 DM (3) both presented with DKA and pancreatic masses, though their CA19-9 levels (30.36 and 251 U/mL, respectively) were lower than those observed in advanced cases such as an 89-year-old female with CA19-9 >121,000 U/mL (14). Similarly, the current patient's CA19-9 (>10,000 U/mL) and CEA (365 ng/mL) align with markers reported in metastatic disease (12, 14) (Table 1).

In addition, imaging findings across cases further illustrate heterogeneity. While the current patient exhibited a 4 cm pancreatic head mass with hepatic metastases, a 70-year-old male had a 2.7 × 5.7 cm pancreatic tail mass with lung and sacroiliac metastases (12), and a 60-year-old male demonstrated a cystic necrotic mass invading the portal and splenic veins (13). In addition, transient symptom relief, such as flank pain with NSAIDs, as seen here, mirrors anecdotal reports of inflammatory modulation in pancreatic cancer (3) (Table 2).

Pancreatic cancer is strongly associated with glucose intolerance, with approximately 80% of patients exhibiting new-onset diabetes or impaired glucose metabolism at diagnosis (2, 3). This phenomenon is attributed to tumor-induced beta-cell dysfunction, insulin resistance, or paraneoplastic effects (3). However, progression to DKA is exceedingly rare in PA, as residual insulin secretion often prevents severe ketosis. Only a handful of cases describe DKA as the presenting feature of pancreatic cancer (3, 8, 9, 12, 13, 14, 15). Our patient's profound hyperglycemia (HbA1c 12.3%) and ketonuria (3+ glucose, 3+ ketones) resulted from type 2 DM and near-complete insulin deficiency due to tumor destruction of pancreatic islet cells, compounded by stress-induced counterregulatory hormone release.

The patient's markedly elevated tumor markers (CA19-9 >10,000 U/mL, CEA 365 ng/mL) and imaging findings – a 4 cm pancreatic head mass with hepatic metastases – align with advanced disease. Notably, her weight loss (23 kg over 2 months) and abdominal pain radiating to the flanks are consistent with pancreaticobiliary obstruction and metastatic burden, as seen in similar cases (2, 3) (Table 1). While DKA-related abdominal pain often mimics acute pancreatitis, the absence of significant lipase/amylase elevation and the presence of hypoechoic hepatic lesions on imaging redirected the diagnostic focus toward malignancy (10, 11).

This case also raises critical questions about screening protocols. The Enriching New-Onset Diabetes for Pancreatic Cancer (ENDPAC) score, a validated tool for identifying new-onset diabetes secondary to pancreatic cancer, incorporates age, weight loss, and glycemic parameters (3). Our patient's rapid weight loss and refractory hyperglycemia would have warranted early imaging, potentially expediting diagnosis. Furthermore, her transient response to NSAIDs for flank and abdominal pain, which inhibit cyclooxygenase-2 (COX-2) overexpressed in pancreatic tumors, may reflect temporary alleviation of tumor-associated inflammation, a phenomenon anecdotally reported in other cases (2).

The literature comparison (Table 1) reveals parallels with prior cases, such as elevated CA19-9 levels (e.g., >121,000 U/mL in Minh V Le's report (14)) and metastatic liver involvement. However, our patient's lack of long-standing diabetes and the acuity of DKA onset distinguish her from cases with chronic hyperglycemia. This aligns with Siddiqui *et al.*'s (8) observation that DKA in pancreatic cancer often arises in individuals without prior prolonged diabetes, suggesting a distinct pathophysiology involving abrupt insulinopenia.

Table 2 Abdominopelvic computed tomography scan findings.

Abdominopelvic CT-scan findings	References
Pancreatic abscess, invading small intestine and the stomach	(2)
Hypodense mass in the body of the pancreas with surrounding necrotic-appearing; lymphadenopathy	(3)
A 2.7 × 5.7 cm mass in the tail and adjacent peripheral body of the pancreas; 1.2 cm nodule in the pancreatic head, innumerable hepatic lesions, 2.2 cm right lower lung mass, and sclerotic lesion of the right sacroiliac joint	(12)
A cystic necrotic mass of 54 × 42 mm dimensions was observed in the head of pancreas; it surrounded the gastroduodenal artery and invaded the portal and splenic veins	(13)
A pancreatic mass measuring about 18.46 mm with metastasis to the liver, adrenal gland, and lungs	(14)
An enlarged edematous pancreas with a hypodensity in the distal pancreatic body concerning for necrotizing pancreatitis and multiple hypodense liver lesions	(16)

Conclusion

In conclusion, while DKA is rarely the herald of PA, clinicians must maintain a high index of suspicion for malignancy in patients with new-onset diabetes, profound weight loss, and disproportionately elevated tumor markers. Early contrast-enhanced imaging and endoscopic ultrasound-guided biopsy remain pivotal for diagnosis. This case reinforces the need for multidisciplinary evaluation of atypical DKA presentations, as timely oncologic intervention may improve outcomes in this otherwise grim prognosis.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the work reported.

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Patient consent

Every effort was made to contact the next of kin of the deceased patient to obtain consent but was unsuccessful.

Author contribution statement

ARK and SG conceptualized the study. YK examined the histopathological analysis. SY composed the initial draft, revised it, and submitted the manuscript.

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