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Pancreatic Cancer Presenting as New-Onset Diabetes

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Key Words
Diabetes · Pancreatic cancer · Diagnosis · Screening

Abstract
Pancreatic adenocarcinoma has an incidence rate nearly equal to the mortality rate and is the fourth leading cause of cancer-related death in the USA. This is largely due to late symptom onset and diagnosis. Evidence has emerged that new-onset diabetes may be a symptom caused by occult pancreatic cancer. We report the case of a middle-aged African American female who presented with hyperglycemia and persistent scapular tenderness. She was subsequently diagnosed with new-onset diabetes and metastatic pancreatic cancer confirmed by liver biopsy. She did not have diabetes or pre-diabetes in the 6 months prior to presentation. The following report will serve to emphasize the role of new-onset diabetes in certain patients as a warning sign necessitating further investigation for pancreatic cancer. New-onset diabetes associated with specific risk factors may prompt for early testing, detection and treatment of pancreatic cancer.

Background

Pancreatic adenocarcinoma has an incidence rate nearly equal to the mortality rate. It is the fourth leading cause of cancer-related death in the USA. This is due to late symptom onset and diagnosis. Long-standing diabetes may increase the risk for pancreatic cancer [1]. Interestingly, some evidence has emerged that new-onset diabetes may be a symptom caused by early occult pancreatic cancer [2, 3].

The pathophysiology behind this association is not well understood. Epidemiologic, clinical, and in vitro studies support the hypothesis that pancreatic cancer-associated diabetes mellitus is a paraneoplastic phenomenon caused by diabetogenic tumor-secreted products [4]. In vitro studies and animal models further suggest that beta cell dysfunction in

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pancreatic cancer leads to an impaired response to oral glucose load, hyperglycemic clamp, and glucagon stimulation [4]. It is possible that new-onset diabetes associated with pancreatic cancer is due to a combination of beta cell dysfunction and an increased insulin resistance [1, 3].

The presentation of pancreatic cancer depends largely on tumor location. Carcinomas in the region of the ampulla and pancreatic head tend to present earliest with signs and symptoms of biliary tree obstruction, while tumors of the body and tail tend to present later as palpable swelling [5]. Other common presenting symptoms of pancreatic cancer are malaise, anorexia, weight loss, and upper abdominal pain. Patients with advanced disease may have an enlarged Virchow's lymph node or ascites [5].

This case report serves to emphasize the role of new-onset diabetes in certain patients as a warning sign necessitating further investigation for a specific etiology, including pancreatic cancer. New-onset diabetes associated with specific risk factors may prompt for early testing, detection, and treatment of pancreatic cancer. This could lead to decreased mortality rates. However, due to the low prevalence of pancreatic cancer, clear guidelines in terms of screening measures even in high-risk patients would be needed. In short, the learning objectives of the present case report are (1) to review the epidemiology and presentation of pancreatic adenocarcinoma, (2) to examine the associations between type 2 diabetes and pancreatic adenocarcinoma, and (3) to illustrate that new-onset diabetes in the setting of risks for pancreatic cancer may be a clue that the patient needs workup for this malignancy.

Case Presentation

A 53-year-old African American female with a medical history significant for stage IB, grade 1 endometrial adenocarcinoma status-post total abdominal hysterectomy and bilateral salpingoophorectomy 7 years ago presented to the Henry Ford Hospital Emergency Department upon instruction from her oncologist after her serum glucose was found to be severely elevated. She had no history of diabetes with fasting blood sugars <126 as recent as 6 months prior to presentation. She led a sedentary lifestyle and had a BMI of 31.8. She was experiencing polydipsia and polyuria for 3 weeks with associated blurry vision and distal extremity paresthesias. Six months prior to presentation, she began experiencing persistent, non-exertional, left-sided chest wall pain. Her pain was managed as an outpatient for several months as costochondritis without resolution. She was a former smoker with a 15 pack-year smoking history. Her family history was significant for type 2 diabetes and hypertension, but she denied a family history of any cancers.

Laboratory findings on admission were significant for serum blood glucose 608 mg/dl, white blood cell count 11.9 K/μl, bicarbonate 27 mmol/l, anion gap 10, and beta hydroxybutyrate 0.13 mmol/l. Serum glycated hemoglobin was 12.7%. Further laboratory studies were significant for an elevated CA 19-9 (349.9 U/ml), normal CA-125 (15 U/ml), and normal C-peptide (1.4 ng/ml). A bone scan for the persistent left-sided chest pain performed shortly after admission was concerning for increased uptake in the left scapula and L5 vertebral body. The patient subsequently underwent a CT scan of the chest, abdomen, and pelvis with IV contrast that showed a 3.6 × 2.5 cm mass extending from the body into the tail of the pancreas and a single 1-cm low attenuation lesion in the liver with minimally enlarged hepatic and portacaval lymph nodes. A biopsy of the hepatic lesion was performed and was suggestive of metastatic pancreatic adenocarcinoma (fig. 1). Pathology showed neoplastic glands surrounded by prominent desmoplastic stroma and lined by cuboidal epithelium

with marked nuclear pleomorphism, loss of polarity, and frequent apoptotic bodies. The tumor cells stained positive for cytokeratin 7 and 19 and stained negative for estrogen receptor and cytokeratin 20.

These findings, along with the newly discovered pancreatic mass, were consistent with stage IV adenocarcinoma of pancreatobiliary origin. After extensive discussion with the patient and her family, she decided to proceed with the FOLFIRINOX chemotherapy regimen for palliative purposes. Her diabetes was treated with a regimen of Lantus 50 units once daily and with Aspart 15 units before meals. She has completed four cycles of chemotherapy and has been experiencing elevated blood sugars despite compliance with her insulin regimen.

Discussion

In our patient, new-onset type 2 diabetes was a harbinger of her undetected pancreatic adenocarcinoma. If it had been detected earlier, it may have prompted clinicians to look more closely for pancreatic pathology in the setting of new-onset bone pain. Her cancer was only discovered after a workup for persistent musculoskeletal pain with nuclear bone scan imaging that showed evidence of metastatic disease. In this case, we cannot definitively state whether pancreatic cancer or diabetes came first, but evidence demonstrates that new-onset type 2 diabetes may be a presenting symptom of pancreatic cancer in some patients [2]. Earlier detection of her diabetes, especially in the context of unexplained musculoskeletal pain and weight loss affecting multiple sites, may have prompted further testing for pancreatic adenocarcinoma. Pancreatic adenocarcinoma carries a poor prognosis since diagnosis is typically made at advanced stages of disease due to delayed onset of symptoms. Recent studies have shown that up to 80% of the patients diagnosed with pancreatic cancer show glucose intolerance, and that pancreatic cancers found at the onset of diabetes are more likely to be resectable [6]. In an attempt to minimize unnecessary testing, patients with new-onset diabetes plus classical risk factors for pancreatic cancer including age, BMI, and family history should be evaluated with blood tests for the tumor markers CEA and CA19-9, both of which have shown a positive correlation with diabetes-associated pancreatic cancer [7]. Screening all patients with new-onset diabetes for pancreatic lesions would not be cost-effective or efficacious, but further research should be done to identify the patients with new-onset diabetes who should be screened further.

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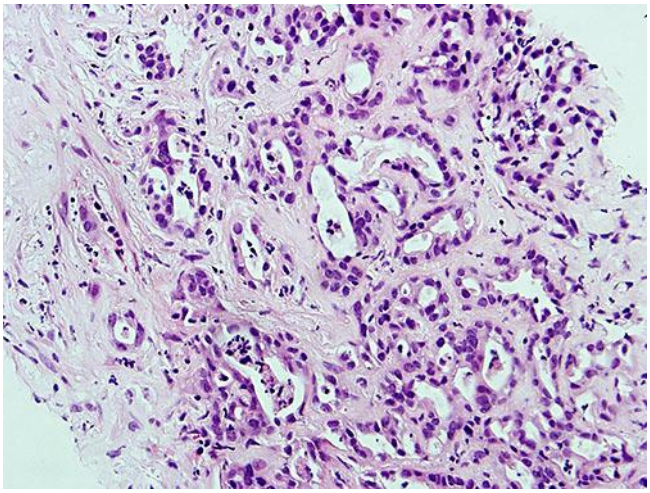

Fig. 1. Liver biopsy of metastatic pancreatic adenocarcinoma. Hematoxylin and eosin stain of the needle core biopsy from the liver mass, demonstrating metastatic pancreatic adenocarcinoma. ×400 magnification.