

Duodenal neuroendocrine tumor and the onset of severe diabetes mellitus in a US veteran

SAGE Open Medical Case Reports
Volume 4: 1–3
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DOI: 10.1177/2050313X15624530
sco.sagepub.com


Lauren Murray¹, Chelsey Haley², Cristóbal S Berry-Cabán² and Almond Toledo¹

Abstract

Objective: Neuroendocrine tumors are neoplasms derived from endocrine cells, most commonly occurring in the gastrointestinal tract. Duodenal neuroendocrine tumors are rare tumors averaging 1.2–1.5 cm, and most are asymptomatic. Common presentation is abdominal pain, upper gastrointestinal bleed, constipation, anemia, and jaundice.

Methods: An adult, Black, male patient with newly diagnosed diabetes mellitus presented to the emergency department with elevated liver function test and fatigue.

Results: Magnetic resonance cholangiopancreatography demonstrated a large obstructing mass (3.6 cm × 4.4 cm × 3 cm) within the second and third portions of the duodenum at the ampulla. Esophagogastroduodenoscopy demonstrated an ulcerated duodenal mass that was biopsied. Immunohistochemical stains were positive for synaptophysin, chromogranin B, and CK7. Chromogranin A was in normal range. Post-Whipple procedure demonstrated a 5.5 cm × 4.1 cm × 2.9 cm duodenal mass with invasion of the subserosal tissue of the small intestine, a mitotic rate of 2 per high-power field, and antigen Ki-67 of 2%–5%.

Conclusion: This case raises the question as to if the patient developed diabetes mellitus due to the tumor size and location or if the new onset of diabetes was coincidental. This case also demonstrates the importance of a proficient history and physical.

Keywords

Duodenal, neuroendocrine tumor, military

Date received: 4 August 2015; accepted: 19 November 2015

Introduction

Neuroendocrine tumors (NETs) are rare tumors constituting less than 5% of all cancers of unknown primary site.^{1–4} The current annual incidence is 3.65 per 100,000 people for the United States.⁵ NETs most commonly occur in the lungs, appendix, rectum, pancreas, and small intestines. They are derived from endocrine cells and frequently secrete a multitude of different hormones or vasoactive substances, depending upon the cell type and location of the tumor.¹ The most common site for NETs is the gastrointestinal (GI) tract, accounting for approximately 73.6% of all NETs; primary duodenal NETs account for only 2.6% of all NETs.^{4,6}

Case presentation

A 52-year-old Black, male, retired US Soldier presented to the emergency department (ED) diagnosed with elevated liver enzymes (aspartate transaminase (AST) 113, alanine transaminase (ALT) 183, and alkaline phosphate 886) by his primary care physician. He had recently worked as a contractor in Afghanistan, Iraq, and Kuwait.

The patient reported significant unintentional weight loss of approximately 13.6 kg during the last 10 months, with the most significant weight loss occurring during the previous 3 months. He reported no decreased appetite but endorsed early satiety as well as increased fatigue, shortness of breath with exertion, increased thirst, visual changes that had subsided, and constipation. He denied having any fevers, chills, nausea, vomiting, and diarrhea; he also denied eating any local Middle Eastern cuisine. The patient did not smoke and did not consume alcohol. His primary care provider diagnosed him with diabetes mellitus.

¹Lake Erie College of Osteopathic Medicine, Bradenton, FL, USA

²Department of Clinical Investigation, Womack Army Medical Center, Fort Bragg, NC, USA

Corresponding Author:

Chelsey Haley, Department of Clinical Investigation, Womack Army Medical Center, 2817 Reilly Rd, Bldg. 2517, Fort Bragg, NC 28310, USA.
Email: chelsey.l.haley.ctr@mail.mil



Admitted to the hospital, the patient's physical examination was unremarkable with the exception of barely visible yellowing of the sclera. A complete metabolic panel showed the following: ALT 457, AST 485, total bilirubin 1.4 (peak total bilirubin 2.1 with direct bilirubin of 1.6), lipase 47, and alkaline phosphate 872. He had a hemoglobin A1C of 13.3%, CA19-9 of 116, and a microcytic, hypochromic anemia.

An ultrasound of the right upper abdominal quadrant demonstrated moderate intrahepatic ductal and common bile duct dilation without visible choledocholithiasis, a distended gallbladder, and findings consistent with hepatosteatosis. Magnetic resonance cholangiopancreatography demonstrated a large mass (3.6 cm × 4.4 cm × 3 cm) located within the second and third portions of the duodenum at the ampulla that was obstructing the intrahepatic ducts, extrahepatic ducts, and the pancreatic duct.

A computerized tomography scan of the chest, abdomen, and pelvis demonstrated a duodenal soft tissue mass that invaded into the uncinate process of the pancreas without gross evidence of additional metastasis. An esophagogastroduodenoscopy demonstrated a duodenal mass with ulceration; biopsies of the duodenal mass demonstrated a NET that stained positive for synaptophysin, chromogranin B, and CK7. The biopsies results were negative for CK20, CBX2, PAX-8, and CD117. Chromogranin A was in normal range. Biopsies of the body and antrum of the stomach demonstrated chronic active *Helicobacter pylori*. Additional staining for somatostatin and calcitonin was performed after the tumor was removed. The biopsy results for both were negative.

The patient underwent a Whipple procedure to remove the tumor. Biopsies from the procedure demonstrated a 5.5 cm × 4.1 cm × 2.9 cm duodenal mass that surrounded, but did not penetrate, the ampulla of Vater, common bile duct, or pancreatic duct. There was invasion of the subserosal tissue of the small intestine, a mitotic rate of 2/10 per high-power field, and Ki-67 of 2%–5%. Samples were negative for gastrin, CA19-9, insulin, and glucagon. All six portal lymph nodes and 13 pancreatic nodes were negative for metastasis. The tumor was histologically a Grade 2 and stage T3N0. After 7 months, the patient has fully recovered with occasional pain in the right flank.

Discussion

Duodenal NETs comprise less than 3% of all duodenal tumors.⁷ These rates are rising due in part to newly developed diagnostic tools. Over 90% of all duodenal NETs are found in the first and second portions of the duodenum, and among these, 20% are in the periampullary region.⁶ The average size of duodenal NET is 1.2–1.5 cm, with more than 75% being less than 2 cm.⁸ According to O'Toole et al.,⁸ regional lymph node metastases are found in 40%–60% of cases. In fact, lymph nodes are the most frequent location of metastasis followed by the liver.⁹

Most duodenal NETs are asymptomatic and hormonally silent.¹⁰ The most common presenting signs and symptoms are abdominal pain (37%), upper GI bleed (21%), anemia (21%), and jaundice (18%).⁵ A duodenal NET in the periampullary area most frequently presents with jaundice (55%). They may also present with abdominal pain, nausea, diarrhea, or vomiting.¹¹ On pathological slides, the well-differentiated tumors typically stain positive for chromogranin A and synaptophysin, whereas the poorly differentiated ones usually only stain for synaptophysin.

The Surveillance, Epidemiology, and End Results Program (SEER) revealed over 35,500 patients with NET from 1973 to 1994; of these, 12% were African American.¹ The mean age for diagnosis of a duodenal NET is 65 years of age; for an African American, it is 59 years of age.

Scherubl et al. suggest that tumors greater than 2 cm should be surgically removed along with the regional lymph nodes even if the imaging is negative for invasion of the regional lymph nodes due to the high rate of lymph node metastasis. Independent risk factors of duodenal NETs to metastasis include invasion of the muscularis propria and the presence of mitotic figures.¹⁰

An adult, Black, male patient with newly diagnosed diabetes mellitus presented to ED with elevated liver function test and fatigue. He was diagnosed with a non-functioning duodenal NET without penetration of the ampulla of Vater, common bile duct, or pancreatic duct, and no malignancy was noted in the pancreatic neck and bile duct margins. Our patient's tumor measured 5.5 cm. Lymph node dissection was negative for metastatic disease in 6/6 portal lymph nodes and 13/13 pancreatic lymph nodes. A tumor size greater than 2 cm is an independent risk factor for metastasis, so it was interesting that this patient had no distal lymph node involvement or metastases.⁶

We reviewed reported literature and were unable to find such a case. This raises the question as to whether the patient in our case report had developed diabetes mellitus due to the tumor size and location or whether the new onset of diabetes was coincidental.

This case demonstrates the importance of a proficient history and physical. Although the patient's abnormal laboratory values were initially what brought him to the ED, the combination of unintentional weight loss, increased fatigue, and decreased exercise tolerance should have signaled a possible malignancy. This emphasizes the importance of being able to put together the symptoms with the abnormal lab values to help lead to the appropriate imaging to help identify the root of the issue.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: The views expressed herein are those of the author(s) and do

not reflect the official policy of the Department of the Army, Department of Defense, or the US Government.

Ethics approval

Our institution does not require ethical approval for reporting individual cases or case series.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Informed consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

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