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Pancreatic Adenocarcinoma in a Patient With Multiple Endocrine Neoplasia 1 Syndrome

To the Editor:

We present the rare occurrence of a concurrent pancreatic neuroendocrine tumor (pNET) and pancreatic ductal adenocarcinoma (PDAC) in a patient with multiple endocrine neoplasia 1 (MEN1)

syndrome. It is important for clinicians to consider the possibility of PDAC in patients with MEN1 because aggressive early surgical intervention provides the only chance of cure.

Multiple endocrine neoplasia 1 is characterized by parathyroid adenomas, pNETs, and anterior pituitary tumors.¹ Multiple endocrine neoplasia 1-associated pNETs are usually slowly progressive and associated with low malignant potential. In the context of MEN1, pancreatic NET size correlates with prognosis and the presence of metastases,² and lesions of more than 2 cm are associated with greater genetic instability and malignant behaviour.³

The European Neuroendocrine Tumor Society recommendations for management of pancreatic lesions in a patient with MEN1 state that early diagnosis and surgical excision of MEN1-related pNET improve survival, preventing or delaying the development of distant metastases.⁴ It is mandatory to operate on MEN1-related non-functioning pancreatic tumors with metastases, size of more than 2 cm, or yearly increased size of more than 0.5 cm. Management of pNETs of less than 2 cm is controversial, current recommendation being intensive surveillance to avoid repeated intervention where lesions are typically multiple and behave in an indolent fashion.

biliary sepsis. Computed tomography (CT) scan and endoscopic retrograde cholangiopancreatography (ERCP) showed intrahepatic and pancreatic duct dilation. Endoscopic stent placement was performed, and the patient improved.

Three months later, his symptoms recurred, and he underwent a further ERCP at which point a blocked stent was replaced with symptomatic improvement. Biochemical testing showed an extremely high carbohydrate antigen 19-9 (CA-19-9) tumor marker of 4520 U/mL (46 U/mL 2 months previously). Cross-sectional imaging showed a 2.8 × 2.2-cm mass in the head/uncinate process of the pancreas with associated duct obstruction. Cytological brushings from the ERCP demonstrated synaptophysin immunopositivity, indicating the presence of neuroendocrine tumor; however, gallium 68 DOTA octreotate positron emission tomography (Ga-68 PET) scanning did not show any uptake in the pancreas. Endoscopic ultrasound demonstrated the double duct sign and confirmed a mass in the head of the pancreas. In view of these findings, in association with a raised CA-19-9, a Whipple pancreatoduodenectomy was performed. Histology demonstrated a 30-mm moderately differentiated ductal adenocarcinoma of the head of the pancreas, invading to the mucosal surface of the duodenum and peripancreatic adipose tissue, pT3 N0 M0 (stage IIA). Also present was a concurrent 9-mm well-differentiated grade 1 pNET, with 5 of 19 lymph nodes positive for metastatic neuroendocrine tumor (pT1 N1). Immunohistochemistry of the pNET was positive for chromogranin and synaptophysin, and Ki-67 was less than 1%. Figure 1 illustrates histopathologic features of both tumors.

CASE HISTORY

A 46-year-old man was under surveillance in a tertiary referral neuroendocrine tumor unit for a diagnosis of MEN1 syndrome. Medical history included Zollinger-Ellison syndrome with resection of primary gastrinoma from the tail of the pancreas, primary hyperparathyroidism, and chronic hypercalcemia.

Fifteen years following his diagnosis of MEN1, he presented with anorexia, nausea, and jaundice and was treated for

DISCUSSION

In this case, the use of serum tumor markers (a significantly raised CA-19-9)

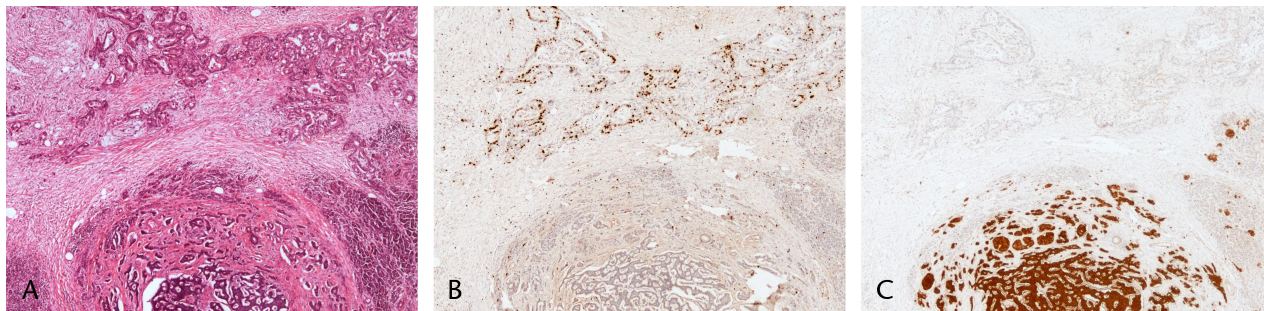


FIGURE 1. A, Hematoxylin-eosin–stained section, original magnification ×4: head of the pancreas with a moderately differentiated pancreatic ductal-type adenocarcinoma (upper half of the picture) closely juxtaposed to a well-differentiated neuroendocrine neoplasm of low grade (lower half of the picture). B, Immunohistochemistry for Ki-67, X4: the proliferative rate with Ki-67 is low in the well-differentiated neuroendocrine neoplasm compared with the high proliferative rate seen in the pancreatic adenocarcinoma. C, Immunohistochemistry for synaptophysin, X4: a diffuse and strong positivity is seen in the well-differentiated neuroendocrine neoplasm, and complete negativity is seen in the adenocarcinoma.

and negative functional imaging (Ga-68 PET) of the pancreatic mass raised the suspicion of an alternative diagnosis to the expected pNET.

CA-19-9 is the most frequently utilized biochemical marker for pancreatic adenocarcinoma, with median sensitivity for diagnosis of 79% (70%–90%) and specificity of 82% (68%–91%).⁵ Specificity falls in jaundice. Recommendations for evaluation of suspected pancreatic adenocarcinoma involve endoscopic ultrasound and CT assessment, and note that CA-19-9 is of limited diagnostic value but of use to guide treatment and follow-up.⁶

The use of functional and somatostatin receptor imaging is important in the evaluation of suspected neuroendocrine tumors; however, all modalities are limited by reduced sensitivity for lesions of less than 1 cm. Gallium 68 PET scan is more sensitive than other modalities; however, its role in the assessment of patients with MEN1 has not yet been determined.⁷ In our case, lack of uptake in the pancreas on Ga-68 PET despite a 3-cm lesion being visualized on CT raised the suspicion of nonneuroendocrine malignancy. The small (9 mm) neuroendocrine tumor was below the resolution threshold of the Ga-68 PET and therefore was not visualized.

CONCLUSIONS

We have presented a rare concurrence of PDAC with pNET in a patient with MEN1 syndrome. This case highlights the importance of relevant imaging and biochemical biomarkers and questions the current practice of surveillance for small pancreatic masses in patients with MEN1 syndrome.

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Masking Effect of Chronic Pancreatitis in the Interpretation of Somatostatin Receptor Positron Emission Tomography in Pancreatic Neuroendocrine Tumors

To the Editor:

The pancreatic neuroendocrine tumors (pNETs) represent a small percentage of all pancreatic tumors (1.3%), but their incidence is rising.¹ Neuroendocrine tumors usually overexpress somatostatin receptors on their cell surface; therefore, somatostatin receptor imaging could be used to evaluate these tumors. Somatostatin receptor positron emission tomography/computed tomography (SMSR-PET/CT) using different somatostatin analogs (such as DOTANOC, DOTATOC, DOTATATE) labeled with gallium-68 is a valuable diagnostic tool for staging and restaging patients with NETs, including patients with pNET.^{2,3}

We present a patient with a multifocal pNET in whom the coexistence of chronic pancreatitis has hampered the correct functional characterization of tumoral lesions at SMSR-PET/CT.

CASE REPORT

A 49-year-old woman underwent magnetic resonance imaging (MRI) for onset of abdominal pain. Magnetic resonance imaging showed a large encapsulated exophytic mass arising from the pancreatic tail, with heterogeneous hyperintensity on axial T2-weighted image caused by necrotic areas. Magnetic resonance imaging also showed smaller lesions distributed in all pancreatic segments that appear variably hyperintense related to cystic components in axial T2-weighted images (Fig. 1). The patient underwent an endoscopic ultrasonography-guided fine-needle tissue acquisition of the largest lesion in the pancreatic tail. Fine-needle aspiration cytology showed small monomorphic cells forming loosely structured groups positive for chromogranin A at immunohistochemistry and highly suspected for NET cells (Fig. 1). Based on the morphologic suspicion of a multifocal pNET, the patient underwent SMSR-PET/CT with gallium-68-DOTANOC for staging. The SMSR-PET/CT images showed diffuse and intense radiopharmaceutical uptake distributed in all the pancreatic segments, and a correct interpretation and functional evaluation of the pancreatic lesions detected at MRI were not possible.