Dull Abdominal Pain Caused by Non-Functional Metastatic Neuroendocrine Tumor

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Vague abdominal pain is a very common and non-specific complaint. Sometimes it may be the only symptom of metastatic malignancy. We present the case of a 68 year old patient with dull abdominal pain and metastatic neuroendocrine malignancy. We provide a detailed description of the imaging modalities and treatment approaches used for this kind of tumor.

Patient Description

A 68 year old man presented to the family physician with complaints of vague abdominal pain of a few months duration, without nausea, vomiting, weakness, weight loss or change in bowel habits. Meticulous physical examination did not reveal any significant findings.

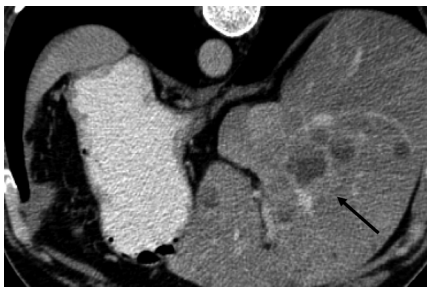
An upper gastrointestinal endoscopy showed normal esophageal, gastric and duodenal mucosa. Abdominal computed tomography [Figure A] demonstrated a pancreatic mass and multiple liver lesions. Percutaneous biopsy specimen from the liver lesions showed solid tumor cells arranged in nests [Figure B]. Each nest comprised large cells with eosinophilic cytoplasm and nuclei without nucleoli. Tumor cells were moderately allomorphic and stained positively with chromogranin and S-100. These morphologic and immunohistochemical features suggested a tumor of neuroendocrine origin. According to the radiologic features the tumor could be regarded as a non-functional neuroendocrine tumor of the pancreas.

Comment

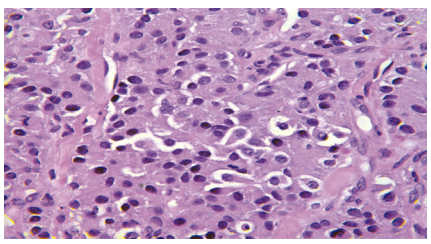
The term "non-functional" or "non-functioning" is a misnomer in the case of neuroendocrine tumors because of the presence of hormone secretion. Tumors considered to be "non-functional" pancreatic neuroendocrine tumors almost always secrete chromatogranins (as in our case) but none is responsible for a specific syndrome.

Pancreatic neuroendocrine tumors constitute a subset of gastrointestinal neuroendocrine tumors that are derived from the widespread neuroendocrine system of the gastrointestinal tract, which is composed of hormone and amine-producing cells. Pancreatic neuroendocrine tumors include insulinomas, gastrinomas, VIPomas, and other rare tumors. Most are slow-growing tumors but proportions are aggressive and there is no correlation between histologic features and biological behavior, because only invasion and metastases establish malignancy. Non-functional pancreatic neuroendocrine tumors comprise approximately 15–25% of all islet tumors and are the third most common islet cell tumor after insulinoma and gastrinoma. They may be sporadic or part of the MEN type-1 syndrome.

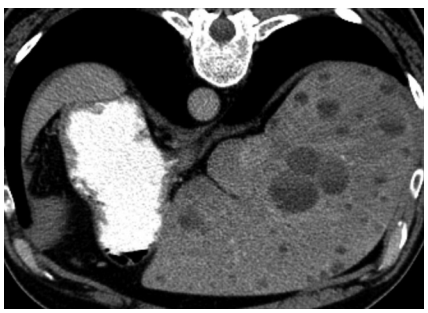
Patients with non-functional pancreatic neuroendocrine tumor usually present late in their disease course with invasive tumors and hepatic metastases. The symptoms are entirely due to tumor invasion or pressure on the adjacent structures. The most common symptoms



[A] Contrast enhanced axial CT image in the portovenous phase shows multiple hypodense lesions in both lobes of the liver.



[B] Percutaneous biopsy specimen showing solid tumor cells arranged in nests composed of large cells with eosinophylic cytoplasm and nuclei without nucleoli (hematoxylin & eosin stain x400).



[C] Post-contrast axial image of the upper abdomen shows multiple hypodense masses in both lobes of the liver that had enlarged as compared to the previous year.

are abdominal pain, jaundice, weight loss, fatigue, or bleeding [1].

The imaging modality for a large non-functional pancreatic neuroendocrine tumors is dynamic contrast-enhanced computed tomography, which usually reveals a solid mass (sometimes with calcifications) isoattenuated to the normal pancreatic parenchyma that enhances post-contrast injection. Most pancreatic adenocarcinomas are hypodense to the surrounding normal parenchyma post-contrast injection on dynamic contrast-enhanced CT [2]. A very sensitive imaging modality for metastatic disease is somatostatin receptor scintigraphy (SRS, OctreoScan®).

A biochemical assay that could help in making the diagnosis of non-functioning pancreatic neuroendocrine tumors is measuring plasma chromogranin A and additional markers such as pancreatic polypeptide [3]. There are two approaches to the treatment of metastatic pancreatic neuroendocrine tumors. The first is the "wait-and-see" strategy that can often be adopted in an asymptomatic patient with a well-differentiated tumor. Possible indications for treatment according to this approach are progressive disease defined as a 25% increase in targeted lesions or the appearance of new disease. A thorough clinical and radiologic follow-up should be done every 3 months. Of course, the appearance of disease-related symptoms is an indication for treatment. The second approach is early treatment in all patients. No prospective randomized study has compared these two approaches [4]. Treatment options for metastatic disease include surgical resection, biotherapy (somatostatin analogues, interferon), and targeted radiotherapy with somatostatin analogues coupled with radionuclides that embolize the target lesions [5].

Our patient was followed for 1 year without treatment. An evaluation of the tumor 1 year later by abdominal CT scan showed no change in the pancreatic tumor size, but enlargement of the liver metastases [Figure C]. Evaluation with somatostatin receptor scintigraphy showed multiple areas of uptake of the tracer in both lobes of the liver, which represent the known multiple metastases with no other sites of uptake, except for the thyroid which might represent other thyroid disease. Due to the worsening of the abdominal pain, treatment with somatostatin analogues was chosen.

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