Imaging of Neuroendocrine Metastases

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Disclosure

• Dr. Blake has received royalties from Springer for books entitled “Adrenal Imaging” and “Imaging in Oncology”

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Goals and Objectives

- Introduction
- Examples of pancreatic and enteric NET metastases
- CT of NET metastases
- MR of NET metastases
- Functional imaging of NET metastases
Introduction

- Gastroenteropancreatic (GEP) NETs - diverse group of neoplasms from cells of diffuse neuroendocrine system (DNES)
- All NETs carry potential risk of malignancy, differ in biology & risk of metastases: more poorly differentiated - more aggressive
- Regional & distant disease: 20-40%. Non-functioning NETs of pancreas & GI tract more likely to metastasize
- Lymph nodes & liver most common sites for metastases followed by lungs, bones, peritoneum and mesentery. NETs can also directly invade surrounding organs such as spleen, stomach, and duodenum
Goal of Imaging

- The presence of liver metastases is an important factor that influences both patient survival & prognosis

- Liver failure is the commonest cause of death, with bowel obstruction & ischemia other less frequent causes

- The goal of distinguishing resectable tumors from unresectable locoregional & metastatic tumors as management & prognosis of these categories differ dramatically
Contrast Enhancement

- NET hepatic metastases usually (>70%) early arterial phase hypervascularity with blood supply from hepatic artery & sometimes exclusively in arterial phase.

- Less frequently show a hypovascular pattern or may rarely demonstrate progressive fill-in like hemangioma (but rim enhancing) or delayed.

- NETs have been reported to demonstrate washout in the delayed phase in > 2/3 of cases.
Primary and Secondary NETs:
Small (< 2 cm) are uniformly arterially enhancing
>2 cm lesions are usually more rim enhancing
Functioning PNET - Gastrinoma

(A) Coronal CE-MDCT images, 54 year old man with Zollinger-Ellison syndrome (ZES) and a large duodenal ulcer. CT demonstrates a 4.8 cm enhancing mass inferior to the uncinate process (large white arrow), low-grade, well differentiated pancreatic NET. Adjacent nodes are pathologically enlarged (arrowheads).

(B) Additionally CECT demonstrates other imaging features of ZES in the GI tract such as thickening of the folds in the stomach, with a polypoid morphology (thin white arrows) and of the jejunal wall (arrowheads). A nasogastric tube is in place in the stomach (curved white arrow in A).
Non-Functioning PNET
56-year-old ♀ with recent history of nausea and vomiting

15x7.5-cm heterogeneous and multilobulated, intensely enhancing mass (yellow arrows) in the pancreas, partially necrotic and completely replacing the parenchyma.

Invasion into splenoportal confluence (blue arrow) with tumor thrombus within portal vein
NET of the ileum

(A) Coronal contrast enhanced CT image of the pelvis demonstrates a 2cm enhancing intraluminal lesion in the distal ileum (curved white arrow), likely the site of the primary tumor.

(B) Axial, arterial phase MRI image demonstrating a focal lesion in segment VIII (straight white arrow), biopsy confirmed NET with suspected intestinal origin (immunohistochemistry positive for CDX-2).
Ileal Neuroendocrine carcinoma

- Mesenteric nodule with focal calcification associated with intense desmoplastic reaction due to lymph node metastasis from ileal neuroendocrine carcinoma.
Progression of disease in the liver after 5 months, with progressive rim enhancement. Status post hepatectomy.

MDCT has an overall mean sensitivity of 82-100% and specificity of 83-100%.
PNET Metastases – CT

Calcified mass in the body of the pancreas (blue arrow - primary NET). Large masses in the liver (yellow arrows) demonstrate heterogeneous peripheral enhancement with some imaging features similar to haemangioma.
Atypical appearances of a PNET metastasis. The lesion is not identified on arterial phase imaging. This lesion is hypoenhancing on the portal venous phase study.
• May be better for small lesions and mets due to contrast resolution & multiphase dynamic imaging

• Overall sens & spec of 74%-94% and 78-100%
  – Alsohaibani Can J Gastroenterol 2008

• Broad spectrum
  – low signal T1 Fat sat
  – bright, intermediate or even low T2 signal
  – Require arterial and portal venous phases post GAD
    • Herwick et al AJR 2006
  – Low signal with hepatobiliary agents on delayed phase
Metastases from islet cell tumors most frequently involve liver and peripancreatic lymph nodes. Signal characteristics of metastases usually resemble those of the primary lesion - prominent enhancement is also typically seen. Central necrosis often occurs as metastases grow.
MRI
58 yo ♀ Poorly Differentiated ileal NET
- The smaller, more anterior lesion is T2 bright and demonstrates arterial enhancement.
- The larger lesion demonstrates some arterial enhancement but is more clearly seen on the portal venous phase image. It is also T2 bright.
53 yo ♂ PNET. Chronic cough, presented with bleeding varices.

An MRI revealed a large mass in the pancreatic tail (yellow arrow), splenomegaly, hilar and gastric varices and a metastasis within the liver (blue arrow).
Small neuroendocrine metastases, some of which are identified on the portal venous phase CT. Many more are identified on the hepatobiliary phase of the post contrast MR.

Rockall AG et al, Neuroendocrinology 2009
McDermott S et al, Clinical Imaging 2013
Metastatic ileal NET in 54 year old man (a, b) Axial contrast-enhanced, arterial phase MDCT images. Pre-treatment scan (a) - large enhancing biopsy proven necrotic, well-differentiated metastatic carcinoid. A lesion in the small bowel was found. The patient was treated with a somatostatin analogue (b). ADC images (c+d). On ADC map acquired pre-treatment the same lesion detected on CT shows low signal intensity due to restricted diffusion (arrow in c). On follow-up increased signal intensity (arrow in d, performed the same day of CT) on ADC with a partial shrinkage is evident.

Liapi et al AJR 2008

On follow-up, shrinkage, necrosis & increased signal intensity on ADC map
Functional Imaging

• $^{111}$In-DTPA octreotide (Octreoscan) most common agent for somatostatin-based radionuclide receptor imaging (SRI)

• Higher sensitivity with SPECT/CT for detecting PNETs, particularly, gastrinomas, nonfunc & func PNETs
  - Less for insulinomas and carcinoids
  - Also limited resolution & uneven biodistribution

• PET/CT Ga-DOTA-Tyr$^3$-octreotide (Ga DOTA NOC) new radiotracer aimed at detecting somatostatin receptors- excellent accuracy - primary 83.4% and metastatic 98.2%
  - Naswa et al AJR 2011
  - Krausz Y et al Mol Imaging Biol 2011
Octreotide

53-yo ♂ with metastatic PNET

NET in the pancreatic tail (blue arrow) with liver metastasis (yellow arrow) on MRI and Octreotide scan
Despite its lower spatial resolution, SRS has a reported high sensitivity (81-96%) & specificity (up to 88%) for hepatic metastases detection. However, detection rates reported in literature are variable. According to some reports, SRS detects more liver lesions per patient than other imaging but other studies have shown MR imaging to depict a far greater number of hepatic metastases. SRS has shown a variable sensitivity (50-70%) for bone metastases, lower than bone scans (90-100%) & MRI (100%).
15 yo ♀ with metastatic insulinoma (2cm in the pancreatic tail – not shown)

Axial contrast enhanced MRI demonstrates a small arterially enhancing lesion in the right lobe. At Octreotide scan performed after MRI no focal area of Indium-111 labeled Pentetreotide uptake within the liver was seen due to ↓expression of somatostatin receptors & ↑background hepatic uptake
PET -FDG
61 yo ♀ well-differentiated metastatic PNET

Usually FDG uptake is ↓ in well differentiated, slow growing PNETs.
FDG useful for poorly differentiated & metastasizing PNETs, which ↓ express somatostatin receptors

Serves as a useful prognostic marker, identifying NETs with an increased risk of aggressive growth patterns such as invasion & metastases

Post Insulinoma resection
Octreotide – negative (in poorly differentiated metastasis due to ↓ expression of somatostatin receptors)

Contemporaneous FDG PET - positive for liver metastasis
Extra-hepatic Metastases

- Bony metastasis (yellow arrow)
- Lymph node metastases (blue arrow)
Conclusions

- Morphologic imaging (CT and MR) widely used to exclude metastatic disease – arterial enhancement is most distinctive pattern
- Molecular imaging (SRS, PET- DOTA NOC) role related to cell membrane ↑expression of somatostatin receptors
- FDG- PET useful for poorly differentiated NETs
- Morphologic and functional imaging techniques play a complementary role in assessment of metastases
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