68GA DOTATATE PET/CT: Multimodality Diagnosis and Treatment of Neuroendocrine Tumors

Presented By:
Kyle Romero, DO, Parker Freels, MD, Savas Ozdemir, MD and Dheeraj Reddy Gopireddy, MD
University of Florida College of Medicine- Jacksonville
A Targeted Approach

- Somatostatin receptors are cell surface proteins that are overexpressed in NETs
  - Part of the G-protein family, which promote intracellular signalling cascades
  - Most commonly seen in gastroenteropancreatic NETs
  - Other tumors that over express somatostatin receptors include pituitary adenomas, pheochromocytomas, meningiomas, paragangliomas, small cell lung cancers, carcinoid, and medullary thyroid cancers

- Traditionally, NETs have been imaged with CT, MRI, and $^{111}$In-DTPA pentetretotide (Octreotide) imaging

- More recently, $^{68}$Ga DOTATATE has been approved for clinical use and allows for a more targeted approach by higher affinity for SSR2 receptors and higher spatial resolution of PET/CT than gamma camera imaging
Normal Biodistribution of $^{68}$Ga DOTATATE

(Organs with increased SST2 gene expression)
$^{68}$Ga DOTATATE PET/CT

- Imaging technique to characterize neuroendocrine tumors (NETs)
  - $^{68}$Ga is chelated to 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) which binds to somatostatin receptors (SSR)

- Normal biodistribution of $^{68}$Ga = all SSR2 expressing organs
  - Pituitary, thyroid, spleen, adrenals, kidney, pancreas, prostate, liver, salivary glands
  - No uptake in the cerebral cortex or heart
  - Low uptake in thymus and lungs

- Highest absorbed dose is to spleen, kidneys, bladder wall, and adrenal glands (critical organs)
  - Estimated Radiation Effective Dose is 0.021 mSv/MBq
  - Administration of 150 MBq (4.05mCi ) to an adult weighing 75kg is about 3.15 mSv
Case 1

77-year-old female who presented to the ED for GI complaints including abdominal cramping and constipation. The patient has a history of prior complex cholecystectomy requiring two open surgeries as well as partial colectomy secondary to colonic volvulus. No history of malignancy.
CT Abdomen & Pelvis at presentation in the ED
7.0 cm primarily cystic structure with solid components and peripheral calcification
within the mesentery adjacent to the right renal fossa, which may represent a mesenteric teratoma.
Five months later, resected by General Surgery
Pathology - Well differentiated neuroendocrine tumor (WDNET), intermediate grade mucinous cystic lesion with low grade dysplasia.

Presurgical CT abdomen/Pelvis
Small hepatic lesion present, which was not present on the preceding study.
Two months following surgery, Nuclear Medicine $^{111}$In-DTPA Octreoscan SPECT/CT and Anterior Planar Image showed 6 lesions within the right lobe of the liver with increased radiotracer uptake and are concerning for metastatic disease from prior neuroendocrine tumor.

Two months later, Hematology/Oncology started Octreotide treatment.
Three months later – $^{68}$Ga DOTATATE PET/CT was obtained

1. Multifocal tracer avid liver lesions, consistent with neuroendocrine tumor metastases.
2. Multifocal tracer avid osseous lesions, consistent with neuroendocrine tumor osseous metastases.
Seven months later, $^{68}$Ga DOTATATE PET/CT was repeated

1. No evidence of recurrent tracer avid mesenteric mass, however, there has been increased radiotracer uptake in the numerous hepatic lesions without definite new lesion identified.
2. Multifocal tracer avid osseous metastases with numerous new osseous lesions.
Given progression of disease, Lutetium-177 Dotatate therapy was recommended.
Case 2

53-year-old female with history of recent partial colectomy and terminal ileum resection at outside facility approximately one week prior for known neuroendocrine tumor presented to the ED with abdominal pain and bloating.
CT abdomen/pelvis with contrast
Ill-defined rounded hypodense region along the proximal falciform ligament. Findings may be related to focal hepatic steatosis however, metastases cannot be excluded based on this examination. Further characterization with liver MRI, liver mass protocol was pursued
Seven months later– MRI Liver Mass protocol
1. Redemonstration of heterogeneously T2 hyperintense, T1 hypointense lesion within the left hepatic lobe measuring approximately 2.0 x 2.6 x 2.7 cm (AP x TRV x CC) with circumferential rim enhancement, without restricted diffusion.
2. There is a T2 hyperintense, T1 hypointense 0.7 cm lesion within segment VI of the liver which demonstrating mild rim enhancement.
There are two discrete foci of increased radiotracer activity within the right lobe of the liver. These lesions correspond with the rim-enhancing liver lesions identified on MRI of the liver. These findings are most consistent with metastatic lesions.
Two months later, surgical resection of the segment VI lesion and open microwave ablation of the lesion in segment IVb

Six months later, $^{68}$Ga DOTATE PET/CT was obtained. Interim resolution of previously noted discrete foci of increased radiotracer activity within segment IV and segment VI. No new foci of increased radiotracer activity to suggest recurrence or new metastatic lesions.
Case 3

63-year-old female status post MVC who received an MRI of the lumbar spine at an outside facility which revealed incidental 1.4 cm cystic lesion within the liver.
CT Pancreas Mass Protocol
9 mm pancreatic neck/proximal body hypodensity is visualized, but too small to accurately characterize by CT. No associated pancreatic ductal abnormalities or further significant findings. Further evaluation with MRI/MRCP imaging with pancreas protocol was pursued.
MRI/MRCP
Approximately 7 mm enhancing lesion correlates with the CT findings and most likely represents a neuroendocrine tumor.
Somatostatin receptor positive pancreatic neuroendocrine tumor. No regional or distant metastasis.
**68Ga DOTATATE PET/CT**

- **Indications:**
  - Initial staging
  - Restaging
  - Detecting metastasis or recurrence
  - Monitoring response to therapy

- However, in a patient in which a NET is suspected (symptomatology, laboratory findings) without confirmed disease, 68Ga DOTATATE PET/CT is not the first line screening exam.

- When compared to 111In-DTPA pentetreotide, 68Ga DOTATATE
  - Has superior diagnostic accuracy (sensitivity = 96% vs. 72%)
  - Emits lower radiation dose (4.3 mSV vs. 12 mSV)
  - Allows for shorter imaging time (one day vs. two day protocol)
Peptide Receptor Radionuclide Therapy

- Targeted Peptide Receptor Radionuclide Therapy (PRRT) for treatment of Gastro-Entero-Pancreatic (GEP) neuroendocrine neoplasms

- Lutetium 177 ($^{177}\text{Lu}$) or Yttrium 90 ($^{90}\text{Y}$)
  - Beta emitting isotopes that cause cellular damage to specific tissues when combined with localizing peptide

- Lutetium 177 has a mean penetration range of 0.67 millimetres in tissue (maximum penetration range of 2.2 mm) which aims to kill targeted cancerous cells with a limited effect on adjacent normal cells
Discussion

- $^{68}$Ga DOTATATE PET/CT allows for a more targeted approach by preferentially binding somatostatin receptors known to be overexpressed in NETs.

- Compared to more traditional imaging techniques, $^{68}$Ga DOTATATE also has superior diagnostic accuracy, emits less radiation, and is more convenient for the patient.

- If NETs can be more accurately identified, treatment can also be tailored to the individual patient through cell targeting peptide similar to somatostatin radiopeptide.
References


