Endocrine Tumor Imaging in the Abdomen: What Your Endocrinologist and Endocrine Surgeons Need to Know

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Disclosure

• I have received royalties from Springer for books entitled “Adrenal Imaging” & “Imaging in Oncology”
Outline and Learning Objectives

• Introduction
• Types of PNETs
• Imaging features of PNETs & metastases
• Types of adrenal lesions
• Imaging features of adrenal lesions
PNET Introduction

- PNETs rare diverse group of related neoplasms & have variable hormone production and secretion
- May originate from APUDomas or multipotential cells - all potentially malignant but differ in risk
- 7% of all GEP-NETs Lawrence Gastro Clin North Am 2010
- Up to 10% of all pancreatic neoplasms Tan World J Clin Oncol 2011, Oberg Semin Oncol 2010
- Equal gender distribution & typical age 51–57 yrs
- Diff types often overlap clinical & imaging features, but also have key clinical and imaging distinctions
Functioning PNETs

- PNETs’ imaging features are direct result of the functioning status => basic classification
- As functioning tumors usually produce symptoms earlier typically small (commonly 1–2 cm) homogeneous tumors
- Most common
  - Insulinoma and gastrinoma
- Less common
  - Somatostatinoma, VIPoma (vasoactive intestinal peptide), glucagonoma, and ACTH–producing tumor
Functioning PNET

Small (< 2 cm) are arterially enhancing

>2 cm lesions can be heterogeneous, ring like

Liver metastases often arterially enhancing
Insulinoma

- Commonest functioning tumor
- ↑ insulin – hypoglycemia, atypical seizures
- Most pancreatic - only 3% peripancreatic tissues
- Equally distributed in pancreas - 10% multifocal
- 90% measure less than 2 cm
- 10% malignant
- Most common met sites: peripancreatic LNs & liver
Insulinoma

• 34-yo ♀ with episodic paresthesias and altered mental status
Gastrinoma

- the second most common type of functioning PNET
- ↑ gastrin
  - ZES=PNET, duo-jej ulceration & ↑ gastric acid
- 60% in pancreas, 30% in duodenum “gastrinoma triangle”
- Multiple 20%–40%
- Somatostatin receptor scintigraphy (SRS) with SPECT
- sensitivity of EUS for duodenal gastrinomas has been reported to be nearly 90%
Gastrinomas
Glucagonoma

- ↑glucagon
- 4D syndrome: diabetes, dermatitis, DVT & depression
- usually >4 cm presentation; >5 cm 60-80% malignant risk
- Almost always in panc body & tail
- Hepatic mets > 50% of patients at diagnosis; mets can also be to adrenals, LNs, bones & lungs

Necrolytic migratory erythema
Glucagonoma

T2W

T1W - post

T1W - post
Other Functioning PNETs

- **Somatostatinoma**
  - ↑ somatostatin – DM, gall stones, steatorrhea
  - large heterogeneous tumors, often malignant
  - 70% in pancreas, and of these, 66% in head

- **Vipoma**
  - ↑ vasoactive intestinal peptide - Verner-Morrison
    - WDHA syndrome
  - large heterogeneous tumors, often malignant
  - 90% in pancreas, and of these, 75% in tail
Non-Functioning PNETs

- Nonfunctioning PNETs present later & are typically large at presentation, averaging 4 cm vs 1.9 cm for func PNETs & also with more mets
- 90% malignant- ↑risk with ↑size
- Large nonspecific heterogeneously enhancing masses – necrosis, and cystic Δs, Ca²⁺ -20% of PNETs & ↑mal risk – Rha Eur J Radiol 2007
- May directly invade surrounding organs/vessels
- Ddx include pancreatic adenoca, mets, & lymphoma
Non-Functioning PNETs

Large (> 3cm), exophytic, heterogenous lesions +/- cystic changes (degeneration). Vascular involvement and metastases +/-

Pfannenberg AC Abd Imaging 2005, Bordeianou L JAC Surgery 2008
Non-Functioning PNET

56-year-old ♀ with recent history of nausea and vomiting.

Differential diagnosis: lymphoma, liposarcoma, GIST

US guided biopsy: well-differentiated PNET
PNET Metastases - MR
Progression of disease in the liver after 5 months.
MEN-1

- Often multiple small PNETs

Thoeni R et al Radiology 2000
CT

• Arterial and portal venous thin collimation phases for diagnosis and follow-up

• Water density contrast is preferred oral contrast to help with small hypervasc tumors adjacent to duodenum

• MDCT advances ↑PNET detection rate from 14-30% (reported in older single slice studies) to currently 69-94% – Rappeport, Acta Radiol 2006, Ichikawa Radiology 2000, Gouya AJR 2003
CT Technique

Arterial

Venous

PNETs

Horton et al
RadioGraphics 2006

Arterial

Venous

Sometimes PV phase better
CT MPRs

33-yo ♂ with VHL family history

MPRs may help in characterization of lesions & allow better localization & better evaluation of surrounding anatomic structures, useful for diagnosis and for surgery planning.
MR

- 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
PNET better seen on MRI

b.

c.
MR DWI

Monitoring with CT & DWI

Somatostatin analogue Rx

Liapi et al
AJR 2008
US

• Transabdominal US limited
  – hypoechoic +/-hyperechoic halo
  – CEUS requires validation

• EUS + FNA
  – ↑Freq probes =>↑resolution
  – Major pancreatic role – Rösch NEJM 1992, McAuley Cl Rad 2005

• Intraoperative US
  – can identify 75- 90% of nonpalpable insulinomas
Cystic PNETs

18% PENs cystic (1/3 purely cystic and 2/3 partially cystic)
Bordeianou L et al. JACS 2008

- Larger (49 vs 23 mm)
- More likely non-functional (80 vs 50%)
- 3.5 x more likely to be part of MEN-1 than solid
IPMN?  PNET
? Mucinous Cystic tumor

Cystic PNET
Hypervascular DDx

RCC

MTC

FNHs
75 yo ♂
hx of RCC
Accessory spleen

81 yo ♂
painful skin lumps
Acinar Cell tumor
Ileal NET better seen with neutral CM
Abdominal NETS

• Morphologic imaging, (MDCT and MR) widely used for initial evaluation & to exclude metastatic disease

• PNETs often arterially enhance but broad spectrum seen with many differences related to functional status

• Morphologic, functional and invasive imaging techniques (EUS, IOUS) play a complementary role
Importance of the Adrenals

- Critical role in physiology and endocrinology
- Critical in oncology - staging
- Incidentaloma dilemma
  - improved imaging - increased detection
    - Berland LL et al JACR 2010
    - Incidentaloma update JACR 2017 (In Press)
Adrenal Mass Classification

- Hyperfunctioning or non-hyperfunctioning

Hyperfunctioning characterized clinically/biochemically

Goal of imaging to differentiate:

- benign “leave alone” mass (e.g., non-hyperfunctioning tumor, myelolipoma, hemorrhage, cyst)
- mass warranting treatment (e.g., metastasis, ACC, pheochromocytoma)
Adenomas

- Small, well defined homogeneous masses of low attenuation
- May show unusual features such as calcification, hemorrhage or necrosis
- Metastases tend to be larger, heterogeneous, and irregular
- But morphologic criteria show a significant overlap
Adenomas

• Intracytoplasmic lipid important in making diagnosis of adenoma with CT or MRI
• Attenuation < 0 HU on an unenhanced CT characteristic of adenoma with 100% specificity, sensitivity 47%
  – Lee et al (Radiology 91)
Low density adenoma < 0 HU

# Pix 245.0
Perim 5.15 cm
Area 2.06 cm²
Avg -5.074 HU
Dev 22.69
Contrast enhanced CT

• Overlap at early I+
• Differences in washout (De-enhancement exploited)
• Enhancement (E) = DYN - NC
• De-enhancement (D) = DYN - DELAY
• Absolute % washout (APW) = D/E x 100
• Relative % washout (RPW) = D/DYN x 100
CT Washout Thresholds

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>RPW</th>
<th>APW</th>
</tr>
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<tbody>
<tr>
<td>10</td>
<td>38%</td>
<td>52%</td>
</tr>
<tr>
<td>15</td>
<td>40%</td>
<td>60%</td>
</tr>
</tbody>
</table>

- Adenomas: RPW 38% 40%
  APW 52% 60%

- < Threshold = Non adenoma = Indeterminate
- Always use APW if available
  - Lipid poor penalized in RPW because their higher NC value is not taken into account

Dunnick & Korobkin AJR 2002
Blake et al Radiology 2006
CT Washout Characterization

- Lipid poor adenomas
- Density $> 10$ HU on non-contrast CT (indeterminate)

Subset of lipid poor washout same as lipid rich
  - Korobkin et al, AJR 2002
  - Pena et al, Radiology 2000

- Pitfalls
  - Hypervascular mets: HCC, RCC  Choi YA et al Radiology 2013
Indeterminate Density Adenoma - CT

55-25/55 = RPW 54.5%
55-25/55-15 = APW 75%

Non-Contrast  Contrast-Enhanced  Delayed

HU = 15  HU = 55  HU = 25
Adrenals on 10 & 15 minute CT washout

10 minute RPW > 38%: APW > 52 %:

- Both had high Sens and Spec (excluding pheos)
- Non Contrast caveats:
  - >43 HU = indeterminate (malignant)
  - <0 HU = benign (supercedes washout)

Blake et al, Radiology 2006

15-minute adrenal protocol RPW > 40%, APW > 60%
% appeared to be more accurate than 10-minute protocol - Sangwaiya et al Radiology 2010

DECT in Adrenals

- VUE images are useful for detection of lipid rich adenoma
- Attenuation measurements on VUE and true unenhanced measurements of adrenal nodules are similar
- Most favorable results are for adrenal masses > 1 cm
- No additional benefit for detection of lipid poor adenoma

Ho et al AJR 2012, Gnannt et al AJR 2012, Glazer et al AJR 2014
Adenoma

- Some report attenuation values of adrenal adenomas based on VNC images are significantly higher >4HU than those obtained with TNC images
  - Botsikas D et al Eur J Radiol 2014
- A lipid-rich adrenal adenoma can thus be confidently diagnosed if the nodule measures less than 10 HU on VNC images
MRI

- Overlap of T1 and T2 intensities
- Similar enhancement
- Washout not routine but feasible
- Chemical shift
  - Lipid protons resonate at slower freq than water
  - OOP signal cancellation within a voxel of lipid and water
3T MRI

• ↑ chem shift at 3T => periodic oscillations between IP & OP occur more rapidly (1.1 ms) than 1.5 T (2.2 ms)

• Posed problems due to inability to breathhold acquire the 1st OP echo at a TE 1.1 ms followed by the first IP echo at 2.2 ms to minimize the effects of T2* decay

• Marin et al overcame this on their 3D sequence using high bandwidth with acceptable SNR
  – Marin D et al. Radiology 2010
  – Nakamura S et al JMRI 2012
Adrenal Adenoma

IP

OOP
Indeterminate - Metastases
Indeterminate

IP

OOP
ACC liver metastases on follow-up
Imaging features of adrenal disorders
Cushing’s Syndrome: Adenoma
Cushing’s syndrome: Adenoma

- With bilateral thin adrenals due to undetectable ACTH
Cushing’s disease: Hyperplasia
Recurrent Cushing's post adrenalectomy due to Nelson's Syndrome with ACTH secreting pituitary macroadenoma priming adrenal rest uptake
Adrenal insufficiency- Hemorrhage

• CT
  – High attenuation (50-70 HU) initially and will decrease in size / density over weeks

• MR
  – Acute - high signal on T1
  – Subacute (> 3 weeks) - ringed on T1,
    • outer hypointense hemosiderin,
    • middle hyperintense methemoglobin &
    • central area of intermediate signal
  – Chronic -hypointense on both T1 and T2
Acute Adrenal Hemorrhage

T1W

T1W FS

T1W FS

T1W +Gad
Hyperfunctioning Neoplasms - Medulla

• Pheochromocytoma
  – 10% bilat, malignant, extra-adrenal (paraganglioma)
  – Syndromes: MEN, NF, VHL
  – NM

• I123-MIBG
• Indium 111-Octreotide
• PET – Hydroxyephedrine
  – FluoroDopa, DotaToc

Pheochromocytoma

T2 bright

Varghese et al, Clin Rad 1997
Hypervascular Pheochromocytoma
• Pheochromocytoma, an Imaging Chameleon
  – Blake et al, Radiographics 2004
Prompt Washout

1/3 of pheochromocytomas mimic adenoma washout

Patel J et al AJR 2013

NC 47HU  DYN 127HU  DEL 64HU
Fat containing Pheochromocytoma

Blake et al, AJR 2003
Pheochromocytoma – Mimic

52 year old man with a left adrenal mass on chest CT

Pheochromocytoma with venous extension on pathology
Adrenal hemorrhage?

Pheochromocytoma
Metastatic Pheochromocytoma
Extra-adrenal Paragangliomas
Hyperaldosteronism

- 40% adenoma
- 60% hyperplasia
- Ca very rare
Hyperaldosteronism

- Adrenal venous sampling lateralizes => adenoma
- Symmetric => hyperplasia
Adrenal Carcinoma

- Irregular shape, inhomogeneous > 4 cm
- Unilateral evidence of invasion, local metastases, calcification and central areas of necrosis. Most T1 hypointense and T2 hyperintense
- Enhance strongly with a slow washout pattern (occasionally atypical)
  - Slattery et al, AJR 2006
  - Zhang et al, Clin Rad 2012
Adrenal Carcinoma

Ax T1W + Gadolinium
Sag T1W + Gadolinium
Adrenal carcinoma
Lesion Morphology

- **Size:** lesions > 4 cm higher risk of malignancy
- **Shape:** irregular shape often malignant (but not always)
- **Lesion heterogeneity:** variable enhancement
Melanoma mets?

immune modulation therapy (ipilimumab)
Melanoma mets?

- Ipilimumab a monoclonal antibody against cytotoxic T-lymphocyte antigen 4
- Biopsy C3 deposits

2/12 interval
Myelolipoma
Myelolipoma

• uncommon, benign tumour usually discovered incidentally (6% incidentalomas – Song AJR 2008)
• Composed predominantly of hematopoietic tissue and adipose cells
• Demonstration of fat virtually diagnostic
• US echogenic masses
• MR hyperintensity on T1 with signal loss on fat suppression
• Some patients may present with retroperitoneal hemorrhage
Pitfalls: Pseudo-adrenal masses:

• Gastric diverticulum
• Posteriorly placed gastric fundus
• Varix
• Tortuous renal or splenic arteries
• Pancreatic, splenic, renal and hepatic masses
• Bowel
• Lymph nodes
Adenomas increasing due to ectopic ACTH from NSC prostate cancer
Conclusions

• Imaging can help characterize many adrenal lesions including most incidentalomas

• Remember adenomas:
  – <10 HU I-, >40% RPW, > 60% APW at 15 min
  – Signal drop on OOP MRI

• Remember pheochromocytomas:
  – often T2 bright & hypervascular but highly variable

• Imaging widely used for initial evaluation of NETs & to exclude metastatic disease

PNETs often arterially enhance but broad spectrum with many differences related to functional status