HEPATOCYTE SPECIFIC
CONTRAST MEDIA:
WHERE DO WE STAND?

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Disclosures

• No relevant disclosures
Outline

• Review of hepatocyte specific contrast media
• Review of hepatocellular carcinoma
• Review of focal nodular hyperplasia (FNH)
• Review of hepatocellular adenoma subtypes
• The trouble begins…
Hepatocyte Specific Contrast Media

- Gadoxetate disodium [*Eovist, Primovist*]
  - Initial extracellular phase followed by 50/50 biliary/renal excretion
- Gadobenate dimeglumine [*MultiHance*]
Hepatocyte Specific Contrast Media

• Uptake
  – Organic anion transporting polypeptides
    • OATP8 (OATP1B3)
    • OATP-C (OATP1B1)

• Excretion
  – Multidrug resistance-associated proteins
    • MRP2 - canalicular
    • MRP3 - sinusoidal
Hepatocyte Specific Contrast Media

- HBP uptake depends on one or more factors:
  - OATP expression
  - MRP expression
  - Presence of functioning bile ducts

Hepatocyte Specific Contrast Media

- HBP hyperintensity due to one or more factors:
  - **OATP** expression
  - **MRP2** expression
  - Mal-located **MRP2**
    - To pseudoglands (some HCC)
  - Abnormal bile ducts

Hepatocyte Specific Contrast Media

• In general, **bad things are dark** on the hepatobiliary phase
  – Non-functioning hepatocytes
  – Decreased OATP8 expression w/ progression of hepatocarcinogenesis
    • May precede neoangiogenesis
• In general, **benign things are bright** on the hepatobiliary phase
• **Lots of exceptions…**
Hepatobiliary agents and their role in LI-RADS

• Washout caution (gadoxetate disodium)
  – Overlap between HBP and equilibrium phases – may get “pseudo-washout” due to early background hepatocyte uptake
  – Call washout only if unequivocal in portal venous phase
Hepatocellular Carcinoma

• Hepatocarcinogenesis (in the cirrhotic liver) generally a relatively scripted process
  – Progressive neoangiogenesis
    • Increasing numbers of unpaired arteries
  – Gradual diversion of venous drainage from hepatic to portal veins
• Progressive loss of OATP transporters during process of hepatocarcinogenesis
• Process accounts for imaging appearance with increasing arterial hyperenhancement, PV washout and hypoenhancement in HBP

Focal Nodular Hyperplasia (FNH)

- Hyperplastic, hypercellular nodule
- Hepatocytes w/o atypia
- Abnormal duct proliferation
- Lack of mature bile ducts
- Central scar with large artery
- Normal background liver
- Believed to be hyperplastic response to vascular abnormality

FNH vs. FNH-like lesions

• FNH-like lesions
  – Arising in abnormal liver
    • FNH occur only in normal liver
• Can look like low-grade HCC (and adenoma)
• May just be inflammatory adenomas…
Hepatocellular Adenomas

• Inflammatory
• Hepatocyte nuclear factor-1α (HNF-1α)-inactivated
• β-catenin activated
• Unclassified
Inflammatory Adenomas

- Used to be classified as a subtype (telangiectatic) of FNH
- Up to 50% of adenomas
- Risk factors: obesity, metabolic syndrome, EtOH
- Higher rate of malignant degeneration (esp. w/ β-catenin mutation)
- Higher rate of hemorrhage

HNF-1α-inactivated Adenomas

- Steatotic adenomas
  - Majority show loss of signal on opposed-phase
- 35-50% of adenomas
- Most common in women on OCPs
- Commonly multiple

β-catenin activated Adenomas

- More frequent in men than other adenomas
- Assoc w/ glycogen storage disease, familial adenomatous polyposis
- Greatest risk of malignant transformation

Unclassified Adenoma

• Everything else….  
• No clear mutational etiology  
• No consistent imaging features
Exceptions to the “bad things are dark, benign things are bright on HBP” rule:
HBP Hyperintense Adenomas

- Agarwal et al.
  - 7 patients, 24 inflammatory adenomas
  - 11 lesions in 4 patients had “classic” imaging features of FNH

- Most likely adenoma subtype to be iso- to hyperintense on HBP
HBP Hyperintense Adenomas

9 year old w/ diminutive portal vein (Abernethy II)

Inflammatory adenoma
HBP Hyperintense Adenomas

• Yoneda et al.
  – Case report of β-catenin activated adenoma
  – Didn’t look like benign lesion on any phase
HBP Hyperintense Adenoma

18 year old
Well differentiated hepatocellular neoplasm w/ β-catenin activation
HBP Hyperintense Adenomas

• Ba-Ssalamah et al.
  – Review of 43 HCAs
  – 6 β-catenin activated adenomas
    • 5 / 6 HBP iso- to hyperintense
  – Most β-catenin activated adenomas and 29% of inflammatory adenomas mimicked FNH (retained on HBP)
HBP Hyperintense Adenomas

11 year old

Inflammatory adenoma w/ β-catenin activation
• 6 studies, 309 patients
  – 397 lesions: 164 adenomas, 233 FNH
    • 257 w/ pathology
    • Molecular subtyping in only 1 paper
• 91 – 100% sensitivity for dx of FNH
  – 95% CI as low as 77%
• 87 – 100% specificity for dx of FNH
  – 95% CI as low as 54%
• Major concern re: bias
• Study that did molecular subtyping had lowest specificity for FNH (87%)
  – Suggests higher specificity in other studies due to misclassification of inflammatory adenoma as telangiectatic FNH
• Study that did molecular subtyping had highest rate of adenomas iso to hyperintense on HBP
  – Range: 0-67%
HBP Hyperintense HCC

• In general HCC appear hypointense on hepatocyte phase

• 6 – 15% are iso- or hyperintense
  – Due to overexpression of OATP8

Hyperintense HCC
- More differentiated
- Lower serum tumor marker levels (e.g. AFP)
- ± less fibrous capsule and hepatic vein invasion
- Less portal vein invasion
- Lower recurrence rate
- ± longer survival
Kitao et. al. Radiology 2012

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What to do?

• If its dark on HBP, view w/ suspicion
  – Except: cysts, venous malformations (“hemangiomas”)

• If imaging features aren’t classic for a benign lesion, be skeptical
  – e.g. the T1 bright “FNH”
  – e.g. the heterogeneously HBP hyperintense “FNH”
What to do?

• Incorporate other information
  – History
    • OCPs, EtOH, Obesity → Adenoma
  – Background liver
  – Growth

• Hypointense rim on HBP or internal mosaic architecture can be helpful signs of HCC

Summary

• Hepatocyte specific contrast media can be a valuable tool in diagnosis of liver lesions

• It's not as simple as HBP bright = benign
SAM Question #1

Which of the following lesions is most likely to be iso- to hyperintense on the hepatobiliary phase when imaged with a hepatocyte specific contrast material?

a) Hepatocellular carcinoma
b) Inflammatory adenoma
c) Metastasis
d) HNF-1α inactivated adenoma
SAM Question #2

Hepatobiliary phase hypointensity of a lesion imaged with a hepatocyte specific contrast material can be explained by which of the following processes:

a) Decreased OATP expression
b) Abnormal background liver
c) Rapid drainage of bile from the lesion
d) Increased blood flow to the lesion
THANK YOU
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