Algorithmic step-by-step approach to assess HCC mimics in a non-cirrhotic liver at 3Tesla

Poster # 60

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Dr. Karthik Ganesan : No disclosures
Learning Objectives

- Review key imaging criteria of HCC in a non-cirrhotic liver
- Review the MR imaging protocol for assessment of focal liver lesions at 3T
- Review a diagnostic algorithm to detect HCC mimics in non-cirrhotic liver
- Review potential pitfalls
**HCC - MR Criteria**

**Major Criteria**
- Arterial Hypervascularity
- Venous Washout
- Delayed enhancing rim
- Follow-up: Interval growth (>50% in ≤6-months)

**Minor Criteria**
- Morphology - Mosaic / nodule-in-nodule
- T2 - Intermediate / Hyperintense
- Fat sparing or Fat containing
- Iron sparing or Hemorrhage
- Restricted diffusion

**HCC mimics - MR Plays a Pivotal Role**

**Road Map for Management**
- Detection & Characterization
- Follow-up of Treated Cases
Imaging Protocol @ 3Tesla

**Injection Buscopan - 0.5mg**
(Hyoscine butylbromide)
Mechanism: antispasmodic
- 5 min before procedure / (Optional)

**MR Advantages**
- Tissue resolution
- Contrast dynamics
- Functional assessment
  (biliary excretion)

**MRI**
- Pre-contrast
  - T2TSE coronal
  - T2TSE axial
  - T1-w dual echo
  - T2TSE obl coronal / sagittal
  - T2TSE obl axial
  - DW (b = 0, 500)
- Post-contrast
  - 3D T1-w GRE
    (HAP - 10-min)
  - T1-w FS axial - 5min
  - T1-w FS cor / sag -optional
  - DW (b = 0, 500)
- Delayed Phase at 60-min
  - 3D T1-w GRE
  - Useful to see GBCA uptake or lack of it
  - Useful adjunct to characterize FLLs

**If CT is used..**
- Temporal resolution
- Calcification in lesion

**CECT**
- Pre-contrast
- Post-contrast AP / PVP
- Delayed Post-contrast

**HCC - MR Criteria**

**Imaging Protocol**

**HCC Mimics**

**Pitfalls**

**HCC - MR Criteria**

**Imaging Protocol**

**HCC Mimics**

**Pitfalls**
HCC Mimics

**T2 hyperintense**
- Simple Cyst
- Complicated cyst
- Cyst with solid nodule
- Solid mass
- Necrotic solid mass

**Diffusion Weighted imaging**
- Prolonged diffusivity
- Restricted diffusivity

**Cyst**
- Complicated / Complex Cyst
- Hemangioma
- Metastases (neuroendocrine)
- IH-CCA (secretory)
- Cystic HCC

**T2 Intermediate / low**
- Solid Lesion

**Homogeneous**
- Diffusion Weighted imaging
- Restricted diffusivity

**Heterogeneous**
- Diffusion Weighted imaging
- Restricted diffusivity

**DCE**
- Homogeneous Enhancement in arterial phase with venous fade

**Additional Features**
- Solitary vs. Multiple
- Background Liver - Storage Disorders
- Assess Spleen & Nodes
- Clinical History of known malignancy
- Tumor Markers - AFP, CEA, CA 19-9, CA-125

**AFP is not raised in one-third of HCCs “Non-secretory HCCs”**

**Biopsy vs. Excision**
- Complex Cyst
- Hemangioma
- IH - CCA
- Metastases
- Focal Nodular Hyperplasia

**B I O P S Y**
- Adenoma
- PEcoma
- Metastases
- IH - CCA
- NHL

**D.D:**
- Hemangiopericytoma
- Hemangioendothelioma
- D.D: Granuloma Pseudotumor
- D.D: Nodular Regenerative Hyperplasia
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**DWI:** Helps to differentiate a T2 hyperintense simple cyst vis-a-vis a complex lesion. Restricted diffusivity may be seen in the entire lesion or its components @ \( b \geq 500 \).

**Differentials:** Complex cyst vs. Cyst with solid component vs. Necrotic solid lesion.

- **T2-w**
  - No restriction @ high b-values. Simple cyst is not an HCC mimic.

- **T2-w TSE**
  - Cyst - No restriction @ high b-values. Simple cyst is not an HCC mimic.

- **T2-w FS**
  - Complex - Restriction seen @ intermediate and high b-values.

- **T1 IP**
  - Cyst
  - Complex lesion

- **T1 OP**
  - Cyst
  - Complex

- **b0**
  - Cyst
  - Complex

- **b500**
  - Cyst
  - Complex

- **T1-w**
  - Complex lesion

- **bD* decay**
  - Complex lesion

- **T2decay**
  - Cyst
**Complex Cystic Lesions**

### Pitfalls

#### HCC - MR Criteria

- Imaging Protocol
- HCC Mimics
- Pitfalls

### Complicated Cyst

- Etiology
  - Hemorrhage within cyst
  - Fibrocalcific cyst

- Features
  - Wall enhancement ±
  - Debris / Fluid level
  - Incomplete / complete septae
  - Non-enhancing mural nodule (retracted blood clot)
  - Biliopathy ±
  - Capsular bulge

- Treatment
  - Asymptomatic: Follow-up
  - Symptomatic: Aspiration
  - Cyst Marsupialization or excision for definitive diagnosis

### Infectious Cyst

- Etiology
  - Cholangitic Abscess
  - Amebic Abscess
  - Hydatid cyst
  - Tubercular Abscess
  - Fungal granuloma

- Features
  - Multiplicity / Solitary
  - Thick walled
  - Enhancing Wall / septae
  - Daughter cysts
  - Intracystic debris
  - Biliopathy ±
  - Subcapsular Rupture
  - THID

- Treatment
  - Treat Primary cause of obstruction
  - PTC / PTBD
  - Antibiotics
  - Aspiration

### Cyst with solid nodule/s

- Etiology
  - Cystadenocarcinoma
  - Neuroendocrine tumor
  - Necrotic HCC
  - Combined / Collision tumor

- Features
  - Solitary
  - Thick walled
  - Enhancing Wall / septae
  - Debris
  - Mural / Papillary nodule
  - Venous invasion ±
  - Biliopathy ±
  - THID

- Treatment
  - CYST Aspiration - poor yield (not preferred)
  - BIOPSY of solid component
  - Excision preferred if possible
  - TACE / Portal Vein Embolization followed by hepectomy / OLT

### Necrotic Solid Mass

- Etiology
  - Necrotic HCC
  - Neuroendocrine tumor
  - Hypervascular metastases

- Features
  - Solitary / Multiple
  - Thick walled
  - Enhancing Wall / septae
  - Intracystic debris
  - Mural nodules
  - Venous invasion ±
  - Biliopathy ±
  - Subcapsular Rupture
  - THID
  - Extrahepatic disease

- Treatment
  - BIOPSY solid component
  - Excision preferred if possible
  - TACE / Portal Vein Embolization followed by hepectomy / OLT
## Pitfalls

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Multiloculated cystic mass with peripheral honeycombed appearance and enhancing low T2 signal solid components with delayed uptake of GBCA into the locules on the hepatobiliary phases.

### Complex cyst with solid components

### DIFFERENTIALS

- Biliary Cystadenocarcinoma
- Necrotic metastases
- Cystic HCC

### Biopsy solid components

Vs. Excision of lesion

### Primary Cystic Neuroendocrine Tumor of Liver

- 0.3% of all primary carcinoids
- Cystic form is rare
- Not an imaging diagnosis
- IHC required: synaptophysin positive
Cavernous Hemangioma

“NO BIOPSY”

- Peripheral Discontinuous Puddling
- Iso-intense to Aorta
- Puddles Coalesce to form Blobs
- Near Complete or Complete Fill-in

Pre-contrast
Hepatic Arterial Phase
Portal Venous Phase
Hepatic Venous Phase
Late Venous Phases

“Progressive Centripetal Enhancement + Incomplete Fill In”
Focal Nodular Hyperplasia

“NO BIOPSY”

Pre-contrast

Hepatic Arterial Phase

Portal Venous Phase

Hepatic Venous Phase

Late Venous Phase

Lesion - early enhancement with venous fade

Vs.

Scar / Septa - late enhancement

“Contrast FADE”
FNH without scar ~ 20% cases

Findings: Solitary, large exophytic intermediate T2 signal intensity mass with restricted diffusivity. Note absence of signal loss on T1-w OP signifying absence of intrallesional fat.
Homogeneous enhancement of the mass is seen on arterial phase, with progressive fade on venous phases, with delayed uptake of hepatocyte specific contrast agent on the hepatobiliary phase image obtained at 60-minutes.

Differentials: Focal Nodular Hyperplasia versus Hepatic Adenoma
Fat containing focal nodular hyperplasia

Focal area of signal loss is seen on the T1 out of phase image in segment 4B (white arrow). Note other areas of signal loss (*) in both lobes. Homogeneously enhancement is seen on arterial phase, with progressive fade and a delayed enhancing scar. Diagnosis: Fat containing Focal Nodular Hyperplasia in a background heterogeneous fatty liver

Teaching Point
- Homogeneous enhancement on arterial phase with venous fade
- Delayed uptake of GBCA in hepatobiliary phase
- Optional findings: Scar/ Septae, Fat, Capsular Retraction
Inflammatory Granuloma - Tuberculosis

- Intermediate T2 signal
- Restricted diffusivity
- Pattern of Enhancement
  a. "Ring / Rim like" with progressive central enhancement
  b. "Homogeneous enhancement with fade"
  c. SPIO uptake - Kupffer cells
  d. May or may not retain Gd-BOPTA or EOB-DTPA
- PET uptake is variable
- Biopsy required for definitive diagnosis
48-year-old woman presented with intermittent right upper quadrant pain. CECT showed multiple enhancing lesions (arrows), one of which showed capsular retraction. MRI showed intense rim enhancement which persisted, with no enhancement of the centre. CT-guided biopsy showed a dense inflammatory infiltrate composed primarily of plasma cells over a fibroblastic background.

Inflammatory Pseudotumor
• Typical Sites: lung, orbit, intestine, mesentery
• Exact etiology: indeterminate
• Histological classification: xanthogranulomatous type, plasma cell granulomas type or hyalinised sclerosing type
• Variable signal on T2-weighted images
• Restricted diffusivity
• Pattern of Enhancement
  a. Hypovascular - most subtypes
  b. Ring / Rim like with non-enhancing core
  c. Nodular enhancement of core
  d. Thick irregular septations / stalactite formation
  e. SPIO uptake ± (due to presence of Kupffer cells)
  f. Capsular retraction
• PET uptake may be variable
• Biopsy required for definitive diagnosis

Ganesan K et al. Capsular retraction: an uncommon imaging finding in hepatic inflammatory pseudotumour. BJR 2009. e256-e260
Hepatic Adenoma

Focal non fat containing hemorrhagic mass in a background fatty liver. The mass demonstrates heterogeneous enhancement on the arterial phase with suspicious washout. Note a central non-enhancing speck and a thin enhancing rim, representing compressed parenchyma / pseudo capsule.

**Diagnosis: Hepatic Adenoma**

**Differential Diagnosis:** AML, PEcoma, HCC
48-year old woman presented with low grade fever since 2-months not responding treatment. Elevated ESR; Liver Function Tests: Normal; AFP / CEA / CA 19-9 are negative. Viral markers are negative. Patient is not on OCs. Screening USG (not shown) detected a focal SOL with heterogeneous echogenicity.

**Findings:** Solitary intermediate T2 signal intensity mass (M) with eccentric areas of low signal. The low T2 signal areas appear hyperintense on T1 in-phase without signal loss on T1 out of phase. Background liver is mildly fatty.

**Interpretation:** Hemorrhagic focal mass in fatty liver.

### PEcoma - Perivascular Epitheloid Cell Tumor

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**Continued**
Findings: Hypervascular mass on arterial phase with venous washout and delayed enhancing rim. 
Differentials: Adenoma
HCC
PEcoma (mesenchymal tumor)

Tumor stained positive with HMB-45 and Desmin

• Zamboni et al described this entity in 1996.
• Recognized in 2002 - 2003 by WHO
• H.P shows “Radial arrangement of cells around a vessel” (perivascular epithelioid cell differentiation)
• Epithelioid to spindle cells with eosinophilic to clear cytoplasm
• Positivity with “Myoid markers” (smooth muscle actin, desmin, calponin, caldesmon)
• Positivity with “Melanocytic markers”: HMB-45, Melan-A, tyrosinase and microphthalmia transcription factor
• Locations: Uterus is the commonest (46% in uterus & 90% female predisposition)
• Benign >> Malignant
• Other entities: AML, clear cell sugar tumor, Lymphangioleiomyomatosis

HCC - MR Criteria
Imaging Protocol
HCC Mimics
Pitfalls

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Pitfalls

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HCC Mimics

- Findings: Hypervascular mass on arterial phase with venous washout and delayed enhancing rim.
- Differentials: Adenoma, HCC, PEcoma (mesenchymal tumor)
- Tumor stained positive with HMB-45 and Desmin

Zamboni et al described this entity in 1996.
Recognized in 2002 - 2003 by WHO
H.P shows “Radial arrangement of cells around a vessel” (perivascular epithelioid cell differentiation)
Epithelioid to spindle cells with eosinophilic to clear cytoplasm
Positivity with “Myoid markers” (smooth muscle actin, desmin, calponin, caldesmon)
Positivity with “Melanocytic markers”: HMB-45, Melan-A, tyrosinase and microphthalmia transcription factor
Locations: Uterus is the commonest (46% in uterus & 90% female predisposition)
Benign >> Malignant
Other entities: AML, clear cell sugar tumor, Lymphangioleiomyomatosis
### Intrahepatic (mass forming) Cholangiocarcinoma: IH-CCA

**Guglielmi A et al.** Mass Forming subtype was associated with negative prognostic factors:
- Extrahepatic bile duct involvement
- Nodal metastases
- Macroscopic vascular invasion
- Perineural invasion
- Higher T stage

#### Imaging Protocol

<table>
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<th>Description</th>
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<td>T1-w IP</td>
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<td>T2 SE</td>
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<td>b=0</td>
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#### Pitfalls

- **HCC - MR Criteria**: Mass forming nodular exophytic
- **HCC Mimics**: Mass forming nodular exophytic

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HCC - MR Criteria | Imaging Protocol | HCC Mimics | Pitfalls

Pre-contrast | Hepatic Arterial Phase | Portal Venous Phase | Hepatic Venous Phase | Late Venous Phase

Pre-HAP | PVP | HVP

3-min | 7-min | 10-min | 60-minutes

“Peripheral Washout Sign”
Hepatic Metastases

Features which aid in diagnosis
- Multiplicity
- Pre-existing Primary
- Extrahepatic disease (other secondaries)
- Absence of macrovascular invasion
- Absence of biliopathy

Hemorrhagic
- Melanoma
- RCC
- Thyroid
- Choriocarcinoma
- Genitourinary (GU)

Target Lesions
- Adenocarcinoma - Lung, Breast, Gastrointestinal (GI), GU
- Small cell
- Neuroendocrine (NET)

Cavitating Lesions
- Adenocarcinoma - GU, Lung
- Squamous cell carcinoma (Head and Neck, GU, Anal Canal)
- Osteogenic sarcoma

Calcifying lesions
- Mucinous Adenocarcinoma - GI
- Osteogenic sarcoma
- Chondrosarcoma
- Prostate Carcinoma
- Parotid Tumors

Differentials
- Hemorrhagic
  - Hepatic Adenoma
  - Angiomyolipoma
  - PEcoma
  - HCC

- Target Lesions
  - Benign
    - IPT
    - FNH
    - Hemangioma
    - Hemangioendothelioma
  - Malignant
    - IH-CCA

- Cavitating Lesions
  - Abscess / Fungal
  - Solitary Necrotic nodule of liver
  - Cystic neoplasms
  - Necrotic HCC
  - Post-treatment metastases, HCC

- Calcifying lesions
  - Granuloma
  - Hemangioma
  - Fibrolamellar HCC - amorphous and associated with non-enhancing scar

Imaging Protocol
- HCC - MR Criteria
- HCC Mimics
- Pitfalls
Findings: Multifocal low T2 signal intensity lesions are disseminated in the parenchyma. The low T2 signal areas appear hyperintense on T1 in-phase without signal loss on T1 out of phase. The nodules appear hyperintense on the pre-contrast 3D T1-w THRIVE image. On the DCE images, the lesions reveal faint enhancement with washout. Subtraction images are extremely useful to depict enhancement in T1 hyperintense (hemorrhagic) lesions.

Interpretation: Multifocal hemorrhagic lesions
Differentials: Hemorrhagic metastases, Hemorrhagic adenoma / PEcoma (less likely), HCC (less likely)

“Diagnosis: Hemorrhagic metastases from malignant melanoma of great toe”

Hemorrhagic Metastases

- Melanoma
- Thyroid
- Renal Cell Carcinoma
- Choriocarcinoma
Target Metastases - “Adenocarcinoma origin”

Both lesions reveal restricted diffusivity on $b=500$.

Metastases shows capsular retraction with “peripheral washout sign” on DCE images.

Hemangioma shows peripheral discontinuous puddles which coalesce with centripetal fill-in on DCE images.

Capsular Retraction
Unique feature of metastases of adenocarcinoma origin.
If solitary, IH-CCA is an important differential for a mass causing capsular retraction.
Necrotic / Cavitating Metastases

34-year-old woman presented with acute onset pain in right hypochondrium. Ultrasonography showed a large cystic lesion with thick irregular margins and incomplete septations. The lesion was considered to represent an abscess. Aspiration yielded no fluid. Pigtail was inserted, which drained copious amounts of altered blood. MRI was performed 3-days later to assess the lesion.
A thick walled hemorrhagic mass (M) is seen in the right lobe with T1 hyperintense contents representing blood degradation products. On DCE images, enhancement of the thick irregular lesion wall is seen.

2nd non-hemorrhagic lesion (M2) in segment 6. The lesion wall shows a continuous rind of thick nodular enhancement, surrounding a hypoenhancing non-hemorrhagic core.

Biopsy showed necrotic metastases from “Endometroid Carcinoma of Uterus”

Teaching Point: Not all necrotic or liquefied masses are abscesses. Further imaging is required to characterize these lesions prior to any planned intervention.
59-year old with a hypoechoic incidentaloma on ultrasonography
Findings: Focal T2 hyperintense reniform shaped lesion with restricted diffusivity on b=500 images. A thin hyperintense rim of fat sparing surrounds the hypointense lesion on the T1-w OP images. It demonstrates a thick blush of peripheral enhancement with a central hypo enhancing core on the arterial phase. On the venous phases, the lesion demonstrates a thin hypoenhancing rim with progressive central enhancement. On the hepatobiliary phase images at 60-minutes, the core reveals retention of GBCA.

Diagnostic dilemma exists in this case

Peripheral Washout with late central enhancement

Delayed uptake of hepatocyte specific contrast at 60-minutes

Malignant lesion
- IH-CCA
- Metastases

Benign lesion
- FNH-like
- Inflammatory
**Teaching Point**

- Retention of GBCA within the lesion on hepatobiliary phase images can mislead the radiologist.
- Infiltrative tumors, such as NHL, may spread over an intact hepatic parenchymal framework. In such instances, presence of functioning hepatocytes interspersed amongst abnormal tissue may lead to retention of hepatocyte specific contrast agents like Gd-BOPTA or EOB-DTPA.
Pitfalls

• This imaging algorithm was proposed on the basis of a single centre study over 5-years. A multicenter study is required to refine and standardize this system.
• Substantial overlap in imaging findings exist which may lead to unnecessary and expensive work-up of HCC mimics.
• In the absence of clinical - biologic markers, no definitive and reliable MR imaging criteria exist to differentiate HCC mimics in these settings:
  a. Complex cystic lesions vis-a-vis Necrotic HCC
  b. Hemorrhagic lesions (Adenoma / PEcoma) vis-a-vis Hemorrhagic HCC
• Though PET-CT has a proven role in evaluating patients with suspected metastases, its role in the initial assessment of primary intrahepatic HCC mimics is not been clearly defined.
• Most malignant HCC mimics (excluding metastases) may always require some form of histopathological confirmation, the current gold standard.
Conclusion

- MR imaging is sensitive and accurate enough to detect & diagnose HCC mimics and guide in appropriate management.
- Liver Biopsy - crucial role in Dx of indeterminate FLLs
- FNA / biopsy in focal solid liver lesions in NCL - issues exist
  a. FNA is unreliable and should “ONLY” be done under image guidance
  b. Targeted biopsy of solid non-hemorrhagic component is necessary
  c. If biopsy is performed, likely incidence of tract seeding must be considered?
  d. If pre-op work-up fails, intraoperative biopsy with frozen section should be done, just in case additional nodal clearance is required.
- Proposed imaging algorithm may serve as a template for development of a comprehensive imaging system to accurately detect HCC mimics in non-cirrhotic livers
References

- van der Hoeff M, Crook DW, Marincek B, Weishaupt D. Primary neuroendocrine tumors of the liver: MRI features in two cases. Abdom Imaging 2004;29:77-81

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