FOCAL LIVER LESIONS IN A NORMAL LIVER

ALEH 2016

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FOCAL LIVER LESIONS IN A NORMAL LIVER

KEY QUESTIONS

▸ Is the liver normal?
▸ Benign vs Malignant?
  ▸ Need for follow up work up?
▸ Differential diagnosis?
▸ Best imaging study?
▸ Do we need a biopsy?
▸ Surgical consultation?
FOCAL LIVER LESIONS IN A NORMAL LIVER

EPIDEMIOLOGY

- Increasing referrals
  - Imaging utilization
  - Imaging quality
- Benign > Malignant
  - Metastases > HCC/CCA
FOCAL LIVER LESIONS IN A NORMAL LIVER

Approach to FFLs

Risk factors for HHC (Hep B, Fatty liver, h/o malignancy, elevated tumor markers, weight loss,

YES

Dynamic CT/MRI (if not performed earlier)

HCC or CCA

Metastasis

Other

NO ("incidentaloma")

Suspect benign lesion

Solid

Hemangioma

Cystic

Dynamic CT/MRI

Central Scar

YES

FNH

NO

HCA/other

Marrero, J ACG clinical guidelines, Diagnosis and management of FLLAm J Gastroenterol  19 August 2014
FOCAL LIVER LESIONS IN NORMAL LIVER

HEPATIC CYST

- Incidental > female
- Asymptomatic
  - Rare RUQ pain
- Imaging fluid filled lesion
- **US, best imaging**
  - No internal echo
  - No or minimal septations
  - No fenestrations
  - No irregular walls
  - No calcifications
  - No doppler flow

Marrero, J ACG clinical guidelines, Diagnosis and management of FLLAm J Gastroenterol 19 August 2014
FOCAL LIVER LESIONS IN NORMAL LIVER

SIMPLE/POLYCYSTIC LIVER DISEASE: MANAGEMENT

- Asymptomatic
  - Conservative
  - No routine aspiration
- Symptomatic cysts
  - Simple
    - De roofing
    - Resection
  - Polycystic Liver Disease PCLD
    - Resection,
    - Liver transplantation

Marrero, J. ACG clinical guidelines. Diagnosis and management of FLLAm. J. Gastroenterol. 19 August 2014
FOCAL LIVER LESIONS IN NORMAL LIVER

BILIARY CYSTADENOMA, CYSTADENOCARCINOMA

- Complexity
  - Septation,
  - Irregular wall,
  - Calcification
- Most are benign

- CT- MRI
- No routine aspiration
  - Limited sensitivity
  - Dissemination risk

- Surgical consultation

HEPATIC HEMAGIOMA

PATHOPHYSIOLOGY, NATURAL COURSE

▶ Most common tumor of the liver (7% on autopsy)
▶ Female predominance 1.5–5 : 1
▶ Possible hormonal dependence
▶ Usually asymptomatic
  ▶ If > 10 cm inflammatory and coagulopathy
    ▶ Kasabach-Merrit Syndrome (KMS)
▶ Types:
  ▶ Capillary hemangioma < 3cm
  ▶ Giant hemangioma > 10 cm
  ▶ Cavernous hemangioma
  ▶ Sclerosed hemangioma

HEPATIC HEMANGIOMA

IMAGING AND DIAGNOSIS

- Ultrasound for typical
  - Homogenous hyper echoic mass, acoustic, sharp margins
- Contrast enhancement for atypical:
  - CEUS, CT, MRI
- MRI with contrast best option
  - Peripheral/globular enhancement on arterial phases
  - Central enhancement on delayed phases
- MRI: 90% sensitivity and specificity

**HEPATIC HEMANGIOMA**

**IMAGING AND DIAGNOSIS CT AND CEUS**

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**Fig. 1. A typical hemangioma adjacent to FNH on MRI and CEUS.**

(A and B) The lesion (haemangioma white arrow) is strongly hyperintense on T2 and hypointense on T1.

(C–E) On contrast-enhanced images, the lesion shows peripheral and discontinuous enhancement followed by complete fill-in on delayed phase imaging. (F–H) The same enhancement is seen on CEUS. Note that the hemangioma is adjacent to a FNH that does not contain a central element.
HEPATIC HEMANGIOMA

IMAGING AND DIAGNOSIS: MRI
HEPATIC HEMANGIOMA

MANAGEMENT

- Typical lesion
  - Conservative
    - Imaging follow up NOT need it
- Pregnancy and OCP are NOT contraindicated
- Refer to MDT
  - KMS
  - Increasing size and symptoms of compression
- Giant hemangioma
  - Liver transplantation for large un-resectable tumor
- Biopsy rarely need it, but NOT contraindicated

FOCAL NODULAR HYPERPLASIA

EPIDEMIOLOGY

- Second most frequent benign liver lesion
- Prevalence 0.03%
  - 90% female, 35-50 y/o
  - Most < 5cm, 20-30% multiple
  - 20% associated to hemangioma
  - Hereditary hemorrhagic telangiectasia
- Pregnancy or OCP Do NOT play a role
- Dystrophic artery, benign appearing hepatocytes

CENTRAL FIBROUS SCAR

FOCAL NODULAR HYPERPLASIA

IMAGING AND DIAGNOSIS

› **Contrast enhancement imaging (CEUS, CT, MRI)**
   - Lesion homogeneity, except in the central scar
   - Strong homogenous enhancement on arterial fase with central vascular supply

› **Central scar**: Enhancement hepatobiliary phase
   - MRI: sensitivity: 70-80% (less in <3cm), specificity: 100%
     - Hepatobiliary contrast increase sensitivity up to 90%
   - CEUS more sensitive in lesion < 3cm
   - Liver biopsy is indicated only
     - Atypical cases on imaging:
FOCAL NODULAR HYPERPLASIA

IMAGING AND DIAGNOSIS CT

- Arterial phase
- Central Scar
- Isointense
- PVP
FOCAL NODULAR HYPERPLASIA

MANAGEMENT

▸ Conservative

▸ Rarely complication

▸ Follow up imaging NOT necessary
  ▸ Underling vascular disease (exception

▸ Refer to MDT
  ▸ Symptoms
  ▸ Pedunculated
  ▸ Exophytic
  ▸ Expanding

▸ Pregnancy or OCP: NOT contraindicated

Suspected FNH

Contrast enhanced imaging – preferably MRI

Diagnosis

FNH - certain

Diagnosis

FNH - doubtful

CEUS

<3cm

Discharge no follow-up needed

Diagnosis uncertain

>3cm

Biopsy

Confirmed FNH

Easl clinical practice guidelines, in press
HEPATOCELLULAR ADENOMA

EPIDEMIOLOGY

- Prevalence 0.002-0.004%
- Female-male 10:1 - 35-40 y/o
- OCP: 30-40 fold increase
- Increase in
  - Males
    - Anabolic steroids
  - Polycystic ovary
  - Klinefelter syndrome
  - Obesity and metabolic syndrome
  - MODY 3 (maturity onset DM3)
  - Iron overload
  - Glycogen storage disease

HEPATOCELLULAR ADENOMA

PATHOPHYSIOLOGY AND NATURAL COURSE

- Proliferation of benign hepatocytes in trabecular pattern and small thin vessels, no bile ducts

- 4 types of clonal benign proliferations
  - Different morphological features and significant complications

  ▶ Hemorrhage
    - Molecular classification
    - Related to tumor > 5 cm

  ▶ Malignant transformations
    - Molecular classification
    - Male

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**HEPATOCELLULAR ADENOMA**

**MOLECULAR CLASSIFICATION**

Table 2. The key features of HCA based on their molecular subtype.

<table>
<thead>
<tr>
<th>Genetic alterations</th>
<th>Pathology</th>
<th>IHC</th>
<th>Clinical</th>
<th>MRI**</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>HNF1-A</em> mutations</td>
<td>Extensive steatosis</td>
<td>LFABP -ve</td>
<td>Adenomatosis, MODY3</td>
<td>Diffuse and homogenous signal dropout on opposed-phase T1</td>
</tr>
<tr>
<td>(30-40%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammatory</td>
<td>Inflammatory infiltration</td>
<td>LFABP +ve</td>
<td>Obesity</td>
<td>Strong hyperintense on T2 and persistent enhancement on delayed phase using extracellular MR contrast agents</td>
</tr>
<tr>
<td><em>Gp130</em> (65%),</td>
<td>Clusters of vessels</td>
<td>SAA (± CRP) +ve</td>
<td>Alcohol consumption</td>
<td></td>
</tr>
<tr>
<td><em>GNAS</em> (5%), <em>STAT3</em></td>
<td>Sinusoidal dilatation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(5%), <em>FRK</em> (10%),</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>JAK1</em> (2%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-catenin mutations*</td>
<td>Cell atypias</td>
<td>LFABP +ve</td>
<td>Male</td>
<td>No specific feature. Often heterogeneous on T1 and T2. No signal dropout on opposed-phase T1</td>
</tr>
<tr>
<td>exon 3 (5-10%)</td>
<td>Pseudoglandular formations</td>
<td>GS +ve (diffuse)</td>
<td>Androgens use increased risk of HCC</td>
<td></td>
</tr>
<tr>
<td>Cholestasis</td>
<td>β-catenin nuclear +ve</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-catenin mutations*</td>
<td>No typical features</td>
<td>GS +ve (faint and patchy)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>exons 7-8 (5-10%)</td>
<td>or inflammatory phenotype</td>
<td>β-catenin nuclear -ve</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unclassified</td>
<td>None</td>
<td>LFABP +ve</td>
<td></td>
<td>No specific Feature</td>
</tr>
<tr>
<td>(5-10%)</td>
<td></td>
<td>SAA/CRP -ve</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>β-catenin nuclear -ve</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* 50% of β-catenin mutated HCA also display inflammatory phenotype.

** Using hepatospecific MR contrast agents and hepatobiliary sequences, most HCA appear hypointense. Yet, some are iso- or hyperintense on these sequences and seem to mainly correspond to inflammatory HCA. Gd-BOPA offers the possibility to evaluate both the delayed and the hepatobiliary phases.

CRP, C reactive protein; GS, glutamine synthase; IHC, immunohistochemistry; LFABP, liver fatty acid binding protein; SAA, serum amyloid A.
HEPATOCELLULAR ADENOMA

HCA INACTIVATED FOR HNF-1A (H-HCA)

- Represent 30-40% of all HCA
- Transcription factor: metabolism and differentiation
- Inactivation of HNF-1A
  - Absence of liver fatty acid binding protein (LFABP)
- Mostly somatic mutation
  - Germline mutation
    - MODY3, Adenomiosis
- Prominent steatosis

HEPATOCELLULAR ADENOMA

INFLAMMATORY ADENOMA (I-HCA)

- 40-55% of all HCA
- Heterogeneous subgroup
  - Activation of JAK/STAT pathway
- Obese and metabolic syndrome
- High alcohol consumptions
- Elevated CRP, fibrinogen levels
- Cluster of small arteries, extracellular matrix, inflammatory cell and sinusoidal dilatation
- IHC: cytoplasmic expresión of serum amyloid A (SAA) and CRP

HEPATOCELLULAR ADENOMA

B-CATENIN ACTIVATED HCA (B-HCA)

- 10-20% of all HCA
- Mutations of B-catenin gen (CTNNB1) exon 3
  - 50% of B-HCA are also inflammatory (JACK/STAT)
  - Males over represented
- HIGH RISK OF MALIGNANT TRANSFORMATION
- B-catenin mutations in exon 7-8: no malignant transformation
- Cellular atypias, pseudoglandular formation and cholestasis
- ICH: Diffuse and strong GS and B-catenin nuclear expression

HEPATOCELLULAR ADENOMA

IMAGING AND DIAGNOSIS

▸ MRI superior
  ▸ Fat,
  ▸ vascular space
  ▸ Heterogenous arterial enhancement

▸ Classified subtypes up to 80%
  ▸ HNF-1A and IHCA classified 90%
  ▸ B-catenin activated HCA,
    ▸ Difficult distinction:
      ▸ Unclassified
      ▸ HCC
HEPATIC ADENOMA

FNH VS HA HEPATOBILIARY CONTRAST

▸ FNH

▸ HA

HEPATOCELLULAR ADENOMA

MANAGEMENT

LIVER CELL ADENOMA: MRI

Male Gender

- Radical management

Female Gender

- Hormonal Therapy cessation

Single lesion

- Size ≤ 5cm
  - Surveillance

- Hemorrhage
  - TAE
  - Persistance > 3 cm
    - Radical management

Multiple lesions

- Size > 5 cm
  - B catenin subtype
  - HNF1 – α subtype
    - Biopsy
    - Surveillance

- Lesions ≤ 5cm
  - Surveillance

Agrawal, S, clinical gastroenterology and hepatology, 13, 2015
HEN TO BIOPSY

- **Early biopsy if:**
  - Equivocal imaging
  - Cannot exclude malignancy

- **Avoid if:**
  - Obvious diagnosis by imaging
  - Most FLL have characteristic MRI/CT/US

- **Risks**
  - Biopsy: bleeding, pain, seeding, false negative
  - Not biopsy: uncertainly, ongoing imaging
WHEN TO REFER TO SURGERY

▶ Symptomatic
  ▶ Exclude other causes

▶ Growing
  ▶ Size > 5 cm

▶ Bleeding

▶ Male sex of HCA

▶ B-catenin HCA
EASL Clinical Practice Guidelines on the management of benign liver tumours

ACG Clinical Guideline: The Diagnosis and Management of Focal Liver Lesions

Jorge A. Marrero, MD, Joseph Ahn, MD, FACG and K. Rajender Reddy, MD, FACG on behalf of the Practice Parameters Committee of the American College of Gastroenterology

Focal liver lesions (FLL) have been a common reason for consultation faced by gastroenterologists and hepatologists. The increasing and widespread use of imaging studies has led to an increase in detection of incidental FLL. It is important to consider not only malignant liver lesions, but also benign solid and cystic liver lesions such as hemangioma, focal nodular hyperplasia, hepatocellular adenoma, and hepatic cysts, in the differential diagnosis. In this ACG practice guideline, the authors provide an evidence-based approach to the diagnosis and management of FLL.

Am J Gastroenterol advance online publication, 19 August 2014; doi:10.1038/aig.2014.213

PERSPECTIVES IN CLINICAL GASTROENTEROLOGY AND HEPATOLOGY

Management of Hepatocellular Adenoma: Recent Advances

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LIVER LESION IN NORMAL LIVER

TAKE TO HOME MESSAGES

▸ Focal liver lesion rising
▸ Conservative management OK
▸ Most die with FLL than from FLL
▸ Know the differential diagnosis
▸ Make the diagnosis
▸ Risk of biopsy and NOT biopsy
▸ Multidisciplinary team
TE ESPERAMOS
ESPERAMOS VOCÊS
WE’LL BE WAITING FOR YOU

MUCHAS GRACIAS

50 AÑOS

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XXV CONGRESO

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