Incidental Focal Liver Lesions
“FLLs” and “Incidentalomas”

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Disclosure

- The speaker regrets he has no conflicts to declare.

YET……..

Objectives

- To characterize the focal liver lesion with confidence as either needing no or only routine follow-up.
- To determine which ones needing further, more rigorous exploration (including biopsy).
- Recognizing the fact that excluding malignancy is paramount.
- Managing some of these focal liver lesions thru primary care practice.
Incidental Liver Lesions

It is important to recognize that the range of diagnoses encountered will be related to the population under study.

Benign conditions such as cholecystitis or renal colic are likely to have findings that mirror those of the general population.

Malignant hepatic lesions will be greater in patients diagnosed with cancer, or disease screen for chronic liver disease.

Thus, the radiographic finding and the clinical context must always be considered together to formulate an appropriate differential diagnosis.

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Incidental Liver Lesions

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Incidence(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td></td>
</tr>
<tr>
<td>• Hemangioma</td>
<td>52</td>
</tr>
<tr>
<td>• FNH</td>
<td>11</td>
</tr>
<tr>
<td>• Adenoma</td>
<td>8</td>
</tr>
<tr>
<td>• Fatty infiltrate</td>
<td>8</td>
</tr>
<tr>
<td>• Other</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>83</td>
</tr>
<tr>
<td>Malignant</td>
<td></td>
</tr>
<tr>
<td>• HCC</td>
<td>6</td>
</tr>
<tr>
<td>• Metastasis</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
</tr>
</tbody>
</table>

FNH = focal nodular hyperplasia; HCC = hepatocellular carcinoma.

Incidental Finding

52% non-cancer patients have benign liver lesion (autopsy)

"Although most incidental findings prove to be benign, their discovery often leads to a cascade of testing that is costly, provokes anxiety, exposes patients to radiation unnecessarily, and may even cause morbidity."

Washington K in: Surgical pathology of the GI tract, liver, pancreas and biliary tract. 2nd ed. 2009; Casarella, WJ Radiology, 2002

Hepatic Cysts

- May be classified as:
  - Developmental
  - Infectious
  - Traumatic
  - Neoplastic
  - Solitary or multiple
  - Adjacent liver tissue is normal and free of fibrosis or inflammation
  - 2-7% of the population
  - Slightly more prevalent in women

Simplified flow chart of imaging techniques used to study incidental liver lesions

- US
- Hemangiomia
- Undetermined
- Dynamic CT
- FNH
- Solid
- Simple Cyst
- Complex Cyst
- CT/MRI
- MIP with specific contrast agents
- MRI with specific contrast agents
- Stop
Hepatic cysts

- Ultrasound is the best imaging method for characterizing these purely cystic liver lesions
- Well-defined homogenous cystic component
- Posterior acoustic enhancement
- Absence of a Doppler signal

Treatment of Hepatic Cysts

- Majority do not require treatment
- Monitor large cysts (>4 cm in diameter) periodically with US to assure that they remain stable
- Laparoscopic unroofing curative for simple cysts
- Enucleation for a cyst adenoma
- Formal hepatic resection for cystadenocarcinomas.

Hepatic Hemangioma

- Most common benign neoplasm of the liver (7% at autopsies)
- Second most common hepatic tumor, exceeded only by the metastases
- Affects all age groups
- Women > men, 1.5-5:1.
- Right lobe of the liver
- Few mm to > 20 cm
- Mesodermal in origin
- Histologically: Blood-filled cavernous vascular spaces of variable size and shape lined by single layer of flat endothelium
- They are usually stable, rarely increase or decrease in size
Hepatic Hemangioma

Characteristic US features:
1. Well-defined, homogenous, hyper echoic lesion
2. Posterior acoustic enhancement
3. No signal on color doppler

Hemangioma MRI

Treatment of Hepatic Hemangiomas

- Asymptomatic patients, particularly those with lesions < 1.5 cm, including those ≤5 cm, can be reassured and observed.
- Rapid growth of a Hemangioma has been reported, justifying close radiological follow up of patient with lesions >5 cm, particularly those in a sub capsular location.
- In the absence of symptoms, the risk of bleeding is too low to justify prophylactic resection.
Treatment of Hepatic Hemangiomas

- Patients who have pain or symptoms suggestive of extrinsic compression of adjacent structures should be considered for surgical intervention (liver resection, enucleation, hepatic artery ligation and liver transplantation).

- Non surgical techniques (hepatic artery embolization, radiotherapy and interferon alpha-2a) mainly in children.

Guess?

Focal Fat vs. Fat Sparing

Focal fatty infiltration  Focal fatty sparing
Focal Nodular Hyperplasia (FNH)

- A benign tumor like lesion containing a *highly vascularised central scar*.
- Predominantly in young females.
- The association with oral contraceptives/estrogens is not clearly established.
- No malignant potential and complications are also exceedingly rare.
- However, FNH shares some imaging features with other primary liver tumors including some of malignant origin (e.g. adenoma, hepato cellular carcinoma (HCC)), and thus a diagnosis of FNH must be unequivocal.

Focal Nodular Hyperplasia (FNH)

- An accurate diagnosis of FNH can be made from an ultrasound study showing:
  - homogenous, solid lesion of variable echogenicity
  - Absence of a peripheral hypo echoic rim (dark capsule)
  - Hyper echoic or hypo echoic central scar, displaying arterial vessels within the central scar on color coded Doppler
  - When in doubt get a dynamic CT or MRI
Focal Nodular Hyperplasia - CT

Focal Nodular Hyperplasia - MRI

Focal Nodular Hyperplasia – Sample Case

36 yr old woman had scanning for abdominal pain
Focal Nodular Hyperplasia – Sample Case

- If any of the features of FNH are lacking from CT or MRI images, a confident diagnosis is precluded and patients must undergo a more invasive diagnostic procedure, preferably a surgical biopsy.

- Image guided percutaneous biopsies can be inconclusive since it may not represent the overall histology of the tumor.

- Surgical removal remains the treatment of choice in the case of an atypical diagnosis of FNH.

Focal Nodular Hyperplasia – Treatment

- The natural history of FNH is one of stability and lack of complications.

- Surgery for:
  - Rare, very symptomatic FNH
  - Highly suspicious lesion, which has eluded diagnosis by all other modalities.

Hepatic Adenoma

- Benign tumor of hepatocellular origin.

- Exceedingly rare compared with the previously described lesions.

- Has a high propensity to bleed, rupture and may undergo malignant transformation.

- Can be difficult to distinguish from an extremely well differentiated hepato cellular carcinoma.
Hepatic Adenoma

Epidemiology:
- 3rd and 4th decade
- Female predominance- 2-6:1.
- Associated with use of oral contraceptives
  - Relative Risk (RR) of 2.5 after 3-5 yrs of use
  - RR 25-40 after 9 yrs of use
- Familial in maturity onset diabetes of the young and glycogen storage diseases, acromegaly, androgen use
- Multiple in 20%, greater than 10 is adenomatosis

Hepatic Adenoma-Molecular Pathology
- Inflammatory- >50%
  - T2 bright
  - + risk of HCC with β-catenin mutation (10%)
- Hepatocyte nuclear factor 1a-inactivated, 35-40%
  - Diffuse fat
  - Very low risk of HCC
- β-catenin-activated, 10%-15%, common in men
  - Absent fat, 45% risk HCC
- Unclassified-non-mutated 5-10%
  - No fat, no inflammation, no increased risk of HCC

Clinical features
- Usually asymptomatic
- May have abdominal pain or discomfort
- Propensity to rupture
  - Intra hepatic hemorrhage and pain
  - rarely hemoptoenceum and shock
- May decrease in size after withdrawal of oral contraceptives
Hepatic Adenoma

Diagnosis is based upon clinical setting, a combination of imaging studies, and/or surgical resection.

A biopsy of aspirate is generally not recommended because of hepatic adenomas are associated with increased risk of bleeding and a needle biopsy is often non-diagnostic.

A common dilemma is the differentiation of a hepatic adenoma from focal nodular hyperplasia.

Ultrasonography: Nonspecific.

Often large and in the right lobe of the liver.

Usually hyper echoic in relation to the surrounding liver parenchyma.

Given the tendency for these lesions to bleed, there is often a central hypo echoic region, which corresponds to hemorrhage.

Contrast enhanced ultrasound may improve accuracy compared with standard ultrasound.

Hepatic Adenoma

Giant hepatic adenoma
Hepatic adenoma with Hemorrhage

NECT - hyper dense (sec. to hemorrhage)  CECT - arterial  CECT - venous

T1 - high signal sec. to hemorrhage  T2 - mixed signal  Gado - poor enhancement

Courtesy Dr. Shweta Bhatt

Hepatic Adenoma – Imaging

Ultrasound showing an hyper echoic lesion  CECT showing intense enhancement

Prompt enhancement of contrast MRI

Hepatic Adenoma

- The natural history and prognosis of hepatic adenomas is not well established. As a result, decisions regarding management of these tumors depend upon symptoms, size, number, location, and certainty of the diagnosis.

- Recommended resection of all symptomatic hepatic adenomas and those > 5cm and before pregnancy.

- Adenomas that do not resolve or enlarge after discontinuation of medication should also be considered for surgical resection after discussion with the patient.
In Western countries, metastatic liver tumors are the most common malignant hepatic neoplasm. In patients known to have extra hepatic malignancy, it is usually necessary to clarify if a hepatic lesion might be metastatic in origin, which typically requires a biopsy. However, histologic confirmation is not always essential if reasonable certainty can be achieved with imaging studies or in settings in which there would be little benefit to the patient to establish a firm diagnosis.
Resectable colorectal cancer metastases are defined simply as tumors that can be resected completely, leaving an adequate liver remnant. Most surgeons would require that there be no radiographic evidence of involvement of the hepatic artery, major bile ducts, main portal vein, or celiac/para aortic lymph nodes and adequate predicted functional hepatic reserve post resection.

Hepato Cellular Carcinoma (HCC)

- History of risk factors for chronic liver disease, viral hepatitis, metabolic liver diseases such as hereditary hemochromatosis, non alcoholic steatohepatitis and alcohol abuse.
- Physical examination: Peripheral stigmata of cirrhosis or decompensated liver disease, which should raise suspicion for HCC.
- The diagnosis can be difficult, and often requires the use of serum markers, one or more imaging modalities, and histologic confirmation.
It can be challenging to distinguish HCC from regenerative or even dysplastic nodules in patients with cirrhosis. MRI is currently the modality of choice in such settings since distinctions can sometimes be made based upon the enhancement pattern and the presence of iron in regenerative nodules.

Hepato Cellular Carcinoma (HCC)

- Serum AFP is normal in the majority of patients with fibro lamellar HCC and in up to 40% of HCC of patients.
- Biopsy is often not required for diagnosis.
- A central scar (typical of focal nodular hyperplasia) can also be seen in patients with fibro lamellar HCC.

HCC Diagnosis

Early enhancement and washout in the arterial phase of hepatic tumor: (A) arterial phase enhancement; (B) early washout; (C) delayed washout.
“Sub-centimeter” liver lesions?

- With increased resolution of CT and MRI has come an increased detection of small nodules: 17% of patients with or without known previous malignancies may display small liver nodules ≤ 10 mm in diameter which are difficult or even impossible to characterize adequately.

- The majority of these small lesions are benign, such as tiny liver cysts or hamartomas, but they can also be malignant.

- Small nodules are generally invisible on most ultrasound examinations.

- It is advisable to obtain a new control examination after about 3-4 months.

- Any intervening growth may justify the use of another diagnostic procedure, such as an image guided percutaneous biopsy.
Incidental Focal Liver lesions: Conclusions

- Incidental liver lesions on medical imaging are relatively common and the vast majority are benign.
- The choice of and need for further investigation when a focal liver lesion is identified depends on several patient factors and characteristics of the lesion on initial imaging.
- Ultrasound is used as a primary screening modality, but in several instances, CT or MRI act as the "problem-solving" technique.
- MRI is superior to CT for focal liver lesion characterization as a result of its high intrinsic contrast resolution and potential use of different types of contrast agents, both specific and non-specific.
- Sub centimeter nodules continue to be a diagnostic dilemma demanding a close imaging examination, which depends largely on the clinical situation of the patient.
- Biopsy may be needed where imaging fails to characterize a lesion adequately.

Thank You

References

- UpToDate: 2012