Liver masses: how to workup a liver mass and update on liver cancer

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BC Surgical Oncology Network, Oct 22 2016
CONFLICT OF INTEREST DECLARATION

I, Alice Wei declare that in the past 3 years:

I have been a member of an Advisory Board or equivalent with the following companies*: Ethicon, Histosonic, Celgene, Sanofi, Takeda, Bayer

I have been a member of the following speakers’ bureau: None

I have done speaking engagements for the following companies*: Sanofi, Celgene

I have received payment or funding from the following companies* (includes gifts, grants, honoraria, and ‘in kind’ compensation): None

I have done consulting work for the following companies*: Cancer Care Ontario

I have held a patent for a product referred to in the program or that is marketed by a commercial organization: None

I or my family hold individual shares in the following companies*: None

I have participated in a clinical trial for the following companies*: None

MANAGING POTENTIAL BIAS

no commercial uses will be discussed

*pharmaceutical, medical device, or communications companies
Learning Objectives

1. review approach for diagnosing liver masses
2. review management of benign lesions
3. review management of malignant tumors
Question: Which of the following statements are true?

1. Liver cysts should be resected if they grow rapidly?
2. Hepatic adenomas should only be resected if symptomatic
3. MRI should be used to assess all liver masses
4. Liver biopsy should be used to confirm diagnosis in all suspected liver cancers
5. Focal nodular hyperplasia can be confused with malignant liver tumours
Approach to liver lesions

- **History & physical**
  - Symptoms?
    - Pain weight loss/ fatigue/ jaundice
  - Risk factors?
    - previous malignancy
    - risk factors for cirrhosis
    - EtoH, PSC etc
    - OCP, anabolic steroid use
- **Routine blood tests** → LFT, Bili, Alb, INR
  - add tumour markers if clinical suspicion
- **Imaging is very important**
  - Diagnostic → multimodality
  - Surveillance → single modality
Imaging modalities

- US $\rightarrow$ CT $\rightarrow$ MRI

- Special tests
  - contrast enhanced US
  - CT/PET

- Nuclear medicine scans
  - RBC scans/sulfur colloid scans $\rightarrow$ obsolete

- Biopsy
  - For indeterminate lesions
What to look for on imaging reports

- **Important features**
  - lesion consistency ➔ was it there before
  - imaging characteristics ➔ enhancement pattern
  - number/location
  - evaluate non-tumour liver

- **Get to know your radiologists**
  - different sensitivity/specificity thresholds
  - variety of area of interest/training
  - dictating styles differ
    - Modifiers used: suggestive, worrisome, cannot exclude...

- **if dictation is not clear**
  - call radiologist for clarification or advice
Ultrasound

- Useful for
  - Screening exam
  - assess for biliary obstruction
  - surveillance of established lesions

- Disadvantages
  - Additional tests required for confirmation
  - Quality is operator dependent
  - Limited visualization in fatty livers
CT scan

- excellent size and anatomic resolution
- IV contrast required
  - Dye protocol depends on pathology
  - Dedicated liver protocol CT needed
- Contraindications:
  - impaired renal function
  - dye allergies
    - can be pre medicated
  - radiation exposure
MRI scan

- Use MRI as confirmatory test
  - for ‘doubtful’ cases
  - No required for surveillance of known lesion
- helpful for ‘indeterminate’ lesions
  - Primovist and/or gadolinium dye
- superior for fatty livers
- MRCP to assess biliary system
When to biopsy

- Biopsy selectively
- Indicated if tissue needed to guide Rx
  - to establish initial diagnosis of malignancy
  - Distinguish primary cancer site
  - Non-tumour liver if liver function an issue
Liver lesions

Liver cyst
Liver metastases
Liver cysts

- >90% asymptomatic
- >50% multiple
- Vast majority are benign
- If symptoms
  - Intra-cystic bleeding/mass effect
  - Consider drainage
- If ↑ growth or complexity consider MRI to characterize
- Polycystic liver disease
  - Assess for extra-hepatic disease
Complex liver cysts

- Often involuted simple cysts appear complex
- Infectious cysts
  - Hydatid cysts
    - Echinococcal cysts
    - Exposure to sheep/dogs
  - Fever and pain may be present
- Neoplastic cysts
  - Biliary cystic neoplasms → rare
  - Cystic metastases occasionally
Solid benign lesion: Hemangioma

- most common liver neoplasm
- 20% population
- F:M 5:1
- always asymptomatic
- 20-30% multiple
- Typical features characteristics
  - sharply demarcated
  - peripheral nodular enhancement
  - centripetal filling
Hemangioma: Work up and treatment

- Ultrasound
  - diagnostic if healthy patient and no risk factors

- CT – liver contrast
  - often diagnostic
  - If classic features present → no F/U needed

- Beware of the atypical hemangioma

- MRI
  - accuracy 85-95%
  - confirmatory test for atypical lesions

- Rx: NO F/U required
Solid benign lesion: Focal Nodular Hyperplasia

- benign, hyperplastic lesion → hamartoma?
- 3% population
- female: male 6:1
- FNH has
  - central stellate scar
  - tortuous feeding artery
  - homogenous arterial enhancement
Focal Nodular Hyperplasia

- FNH can be confused
  - adenoma
  - fibrolamellar HCC
  - Typical HCC

- US and CT are NOT diagnostic
- FNH must be confirmed with MRI
- MRI accuracy 70-90%
- sometimes biopsy needed
Solid benign lesion: Hepatic adenoma

- benign hepatocyte tumour
  - uncommon 1/10^6 - 4/10^5
  - 44% have symptoms
  - 30% multiple
  - Premalignant (β-catenin mutation)

- associated with
  - OCP use / anabolic steroids
  - obesity
  - storage diseases (Glyogen Storage Types 1 And 3)

- ** potential for rupture and malignant transformation

- MRI to characterize

- biopsy usually required
Solid benign lesion: Hepatic adenoma

- **Treatment**
  - Stop exogenous hormones
  - Refer for surgical resection
    - If bleeding → urgent embolization +/- surgery
  - Expectant management an option for small adenomas
    - < 3 cm, no high risk features (beta-catenin mutated, inflammatory, undifferentiated subtype, hypervascular)
    - Surveillance → Imaging and AFP q6 mo X 2 yrs, then qyr
  - Treatment for > 3cm
    - Ablation, RFA, resection

Solid malignant lesion: Metastases

- most common malignancy in liver
- often multiple
- appearance depends on primary
  - most hypoattenuated: adenocarcinoma
  - hypervascular: neuroendocrine, renal, melanoma, other

- workup depends on clinical setting
  - often biopsy NOT required for new lesions in recent cancer patient

- Treatment depends on primary cancer
Solid malignant lesion: Hepatocellular carcinoma

- Increasing incidence due to
  - Hep C, fatty liver disease (NASH)
  - Improved screening for cirrhosis
- Majority have liver disease
- Hyperplastic → dysplastic → malignant
- Difficult to differentiate between dysplastic nodule and HCC
- Usual variants have atypical imaging
  - HCC-cholangiocarcinoma variant
    - Atypical imaging
    - Worse prognosis
- Fibrolamellar HCC
Hepatocellular carcinoma

- Imaging characteristics
  - Signs of cirrhosis
  - Arterial enhancement with venous ‘washout’
  - Often multifocal

- Typical imaging + AFP are definitive
  - Biopsy often NOT required

- Rx: depends on liver function and tumour stage
  - Surgery only for Childs A, no portal hypertension
Management of HCC: BCLC algorithm

Very early stage (0)
- Single <2 cm
- Child-Pugh A, PS 0
  - Potential candidate for liver transplantation
  - No
  - Yes
    - Portal pressure
    - Bilirubin
      - Normal
      - Increased
        - No
        - Yes
          - Ablation
          - Resection
          - Transplant
          - Ablation

Early stage (A)
- Single or ≤3 nodules <3 cm
- Child-Pugh A–B, PS 0
  - Single
  - ≤3 nodules
  - Associated diseases
    - No
    - Yes
      - Ablation
      - Resection
      - Transplant
      - Ablation

Intermediate stage (B)
- Large multinodular
- Child-Pugh A–B, PS 0
  - TACE

Advanced stage (C)
- Portal invasion
- Extrahepatic spread
- Child-Pugh A–B, PS 1–2
  - Sorafenib

Terminal stage (D)
- Child-Pugh C, PS 3–4
  - BSC

Curative treatments
- Ablation
- Resection
- Transplant
- Ablation

Palliative treatments
- TACE
- Sorafenib
- BSC
Solid malignant lesion: cholangiocarcinoma

- usually single hypoattenuated lesion

- Klatskin type if jaundice and biliary obstruction at bifurcation

- US/CT/MRI suggest adenoCA

- metastatic W/U usually required
  - CT chest, OGD/, colonoscopy, mammogram

- biopsy may be required
  - IHC → CK-7 + positive, CK 20-
Cholangiocarcinoma treatment

- Treat jaundice +/- cholangitis if present
- Surgical resection if resectable
- Role of adjuvant chemo +/- XRT
  - No good evidence
  - Gem/Cis considered for Stage III
  - XRT if positive margins
- Liver transplantation (Mayo protocol)
  - < 3cm localized klatskin tumour
  - Unresectable or liver disease
## Radiologic features of common liver lesions

<table>
<thead>
<tr>
<th></th>
<th>US-US Doppler, Contrast Ultrasound</th>
<th>Triphasic CT</th>
<th>MRI</th>
<th>PET Scan</th>
<th>CT-Angiography</th>
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</thead>
<tbody>
<tr>
<td><strong>Hemangioma</strong> (1-10 cm)</td>
<td>Hyperechoic</td>
<td>+</td>
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<td>Doppler: low flow, low index, absence of spectral broadening</td>
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<td>Peripheral puddles, fill in from periphery, enhancement on delayed scan</td>
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<td>Peripheral enhancement centripetal progression</td>
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<td>Hyperintense on T2, hypo intense on T1</td>
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<td>SS &gt; 95%, SP 95%</td>
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<td>Cotton wool pooling of contrast, normal vessels without AV shunt, persistent enhancement</td>
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<td><strong>Focal fatty liver</strong></td>
<td>Hyper echoic, no mass effect, no vessel displacement</td>
<td>++</td>
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<td>Sharp interface</td>
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<td>Low density (&lt; 40 u)</td>
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<td>Normal finding</td>
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<td><strong>FNH (&lt; 3 cm)</strong></td>
<td>Homogenous iso, hypo, or hyper echoic, central hyper echoic area</td>
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<td>Central arterial signal</td>
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<td>Hyper vascular 70% centrifugal supply</td>
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<td>Doppler: high flow, spectral broadening</td>
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<td>Homogeneous enhance strongly with hepatic arterial phase</td>
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<td>Isodense with liver; Central low density scar</td>
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<td>Hyper vascular +Gd</td>
<td>Isodense T1</td>
<td>Hyper intense scar T2</td>
<td>Hyper intense in T1 (intra lesional fat)</td>
<td>No uptake if degeneration to HCC</td>
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<td>SS &gt; 95%; SP &gt; 95%</td>
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<td><strong>Adenoma</strong> (5-10 cm)</td>
<td>Heterogeneous echoic</td>
<td>+++</td>
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<td></td>
<td>Hyper echoic</td>
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<td>Hyper vascular</td>
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<td>If haemorrhage: anechoic center</td>
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<td>Large peripheral vessel</td>
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<td>In doppler: variable flow, spectral broadening</td>
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<td>Central scar if haemorrhage</td>
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<td>Homogenous &gt; Heterogeneous, Peripheral feeders filling in from periphery</td>
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<td><strong>HCC</strong></td>
<td>Hypo or hyper echoic</td>
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<td>Doppler: hyper vascular</td>
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<td>Hyper vascular</td>
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<td>Hyper vascular, often irregular borders</td>
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<td>Av shunting</td>
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<td>Heterogeneous &gt; Homogeneous abnormal internal vessel</td>
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<td>Angiogenesis</td>
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<td>Hallmark is venous washout SS 52%-54%</td>
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<td>Poor different: Hyper intense T1, Hyper intense T2</td>
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<td>show no uptake at PET</td>
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<td>Well different: Hyper intense T-1, iso intense T-2</td>
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<td>SS 53%-78%</td>
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<td><strong>Cholangiocarcinoma</strong></td>
<td>bile duct dilatation if major ducts are involved. Intra-hepatic CCC: no bile dilatation</td>
<td>Hypo dense lesion: Delayed enhancement</td>
<td>Hyper intense T1</td>
<td>Uptake ++</td>
<td>Hypervascular</td>
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<td>Doppler: hyper vascular</td>
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<td>Doppler: index and flow high, spectral broadening</td>
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<td><strong>Metastasis</strong></td>
<td>SS 40%-70% hypo to hyper echoic, doppler: low index and flow, presence of spectral broadening</td>
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Treatment with liver surgery

- HPB sub-specialization
- Surgeons now better oncologists
  - collaboration with cancer centers
  - use of neo-adjuvant therapy
- advanced technical toolbox
  - high volume experience
  - vascular resections now routine
  - minimization of complication rates

---

HPB surgery in Ontario

HPB Cancer Surgery Standards
Number of liver cancer surgeries by hospital corporation, fiscal years 2004/05 vs. 2014/15

Designated centre volume requirements: 30 liver resections
(50 total HPB surgeries of which a minimum of 20 must be pancreatic)

Liver surgery target

Ontario volume
2004/05: 385
2014/15: 770

Report date: July 2015
Data source: CSQI methodology, Discharge Abstract Database (CIHI) and National Ambulatory Care Reporting System (CIHI)
Prepared by: Cancer Care Ontario, Cancer Informatics
Notes:
* indicates designated centre
^ In 2010/11 St. Joseph’s Healthcare Hamilton performed HPB surgery in partnership with Hamilton Health Sciences as a temporary measure until the standards could be fully implemented at one site. In 2011/12 HPB surgery has been consolidated
Conclusions

- Liver masses are commonly identified.
- Imaging usually distinguishes between benign/malignant.
- Selective biopsy for indeterminant lesions or when tissue is required for Rx.
- Liver resection should be performed at an experienced centre.